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# ABSTRACTS OF WORLD MEDICINE

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This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals* and in *World Medical Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together under the same heading. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

ABSTRACTS OF WORLD MEDICINE

VOL. 15 NO. 6 JUNE, 1954

# Pathology

## EXPERIMENTAL

1526. **Some Special Features of the Course of Pulmonary Infection Associated with Trauma of the Brain.** (О некоторых особенностях течения инфекционного процесса в легких при травме головного мозга) D. S. SARKISOV and L. Y. ÉBERT. *Архив Патологии* [*Arkh. Patol.*] **15**, 26–33, Nov.–Dec., 1953. 6 figs., 12 refs.

Pneumonia was induced in two groups of cats by the intratracheal introduction of a suspension of *Staphylococcus aureus* in plastic, the brain in one group being traumatized and in the other left intact. The lungs were studied histologically after varying intervals, and the course of the infection compared in the two groups. In the animals with brain damage the pneumonia assumed a haemorrhagic or confluent lobar form in contrast to the more discrete and purulent lesions found in the controls. Moreover, some of the animals with damaged brains failed to develop any reaction whatever, although the dissemination of the infecting organisms was verified by culture. The experiments suggest that not only the origin, but also the course and character, of inflammatory processes in the lungs are determined by the state of the whole organism, and particularly of the nervous system. *L. Crome*

1527. **Investigations into the Chemical Nature and Properties of "Necrosin" (Macrocytase) and of Haemolysin in Inflammatory Exudates.** Исследование химической природы и свойств «некрозина» (макроцитаза) и гемолизина воспалительных экссудатов) V. Z. GORKIN. *Архив Патологии* [*Arkh. Patol.*] **15**, 13–26, Nov.–Dec., 1953. 4 figs., 26 refs.

"Necrosin", one of the substances isolated by Menkin and regarded by him as responsible for the clinical features of inflammation [see *Lancet*, 1947, **1**, 660; *Abstracts of World Medicine*, 1947, **2**, 260], was extracted by the author from inflammatory exudates by a process involving dialysis with saline, which partly eliminates the protein of desoxyribose nucleic acid, the residue being then fractionated with ammonium sulphate and the deposit purified by Morton's butanol extraction technique, the necrosin passing into the water phase. The resulting solution was turbid, but yielded a clear supernatant fluid containing protein after centrifuging for 20 minutes at 6,000 r.p.m. Most of the necrosin could be thrown down out of this solution with ammonium sulphate at 0·35 to 0·5 saturation. Purified necrosin has therefore the properties of pseudoglobulin, and not of euglobulin as stated by Menkin.

The necrosin thus obtained was subjected to biological and chemical tests and was found to be identical in its properties with the macrocytase of Metchnikov. It is a proteolytic, and particularly fibrinolytic, enzyme of the trypsinase type with optimum activity at *p*H 7·7 to 8·2. Metchnikov believed that macrocytase had haemolytic properties; the present investigation showed, however, that the substance responsible for haemolysis merely accompanies necrosin and can be separated from it by ether or butanol. It appears to be an unsaturated fatty acid. The high specific activity of the purified necrosin and its electrophoretic features suggest that it contains few inactive components. An anti-necrosin serum which permits the quantitative estimation of circulating necrosin has been obtained experimentally, and further work on this is in progress.

The results suggest that the greater part of the necrosin present in inflammatory exudates is bound to insoluble cells and cellular debris, and its increase corresponds to the proliferation of macrophages in the fluid. Menkin's suggestion that necrosin plays an exceptionally important part in the pathogenesis of inflammation is therefore considered to be unjustified, and his theory of inflammation is further criticized on account of its emphasis on local changes without regard to the effects of the general regulating systems of the organism, and particularly of the central nervous system. *L. Crome*

1528. **An Experimental Study of Some Pressure Effects on Tissues, with Reference to the Bed-sore Problem** T. HUSAIN. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] 66, 347–358, Oct., 1953. 16 figs., 30 refs.

An investigation is reported from University College Hospital Medical School, London, into the effects of short periods of pressure on the skin and underlying tissues and on their susceptibility to infection. Pressures of 100 to 800 mm. Hg were applied for periods of 1 to 10 hours to the tails of rats by means of a plethysmograph, and to the legs of rats and guinea-pigs by means of a pressure cuff. Stained paraffin sections of the skin and underlying muscle from the compressed areas were then examined microscopically and preparations were also made to show the vascular pattern in the leg muscles and skin of the rat.

It was found that a low pressure maintained for a long period caused more damage to the tissues than a high pressure for a shorter period, the lesions including de-

generation and necrosis of muscle similar to that seen in tissue removed from 10 patients with bed sores. Increased capillary permeability on release of the pressure was demonstrated by injecting 1% trypan blue solution intravenously in rats just before the application of pressure, and it is suggested that this accounts for the localization of infection at the site of pressure which occurred when streptococci were injected intravenously at the time of compression, large abscesses being present in the tissues 3 days later.

In another series of experiments it was shown that mild, localized compression of a degree insufficient to cause tissue changes in the normal rat's leg might cause severe tissue damage if applied after partial obstruction of the arterial supply to the part, division of its main nerve supply or transection of the spinal cord, or in the presence of a deficiency of ascorbic acid. It was also shown that pressure impairs the functional capacity of muscle as well as causing morphological changes, and this in turn may reduce its blood supply. The relation of these findings to the causation and prevention of bed sores is discussed. *A. Wynn Williams*

1529. **The Formation of " Antirenin " during the Prolonged Intravenous Administration of a Renin Preparation in Dogs.** (Об образовании «антеренина» при длительном внутривенном введении собакам препарата Ренина)
N. T. Kovaleva. *Архив Патологии* [*Arkh. Patol.*] **15**, 38–43, Nov.–Dec., 1953. 3 figs., 9 refs.

Renin ceases to exert its hypertensive effect in dogs after repeated administration, the period of effectiveness varying with each animal, and a renin-neutralizing substance, " antirenin ", appears in the blood during this non-reactive state. If the administration of renin is stopped, its hypertensive effect is restored after a time, but the amount of renin required to induce the non-reactive state becomes progressively smaller. It is argued that the production of antirenin is one of the manifestations of a general defence reaction of the organism in which the leading part is played by the nervous system. *L. Crome*

1530. **Experimental Production of Carcinoma with Cigarette Tar**
E. L. Wynder, E. A. Graham, and A. B. Croninger. *Cancer Research* [*Cancer Res.*] **13**, 855–864, Dec., 1953. 22 figs., 42 refs.

A review of some of the previous attempts made since 1928 to induce the growth of tumours experimentally in laboratory animals by means of various tobacco products (the essential findings of which are given in a table) shows that only 7 epidermoid cancers of the skin of mice have so far been produced in this way.

In the present study, carried out at the Memorial Center for Cancer and Allied Diseases, New York, a tar condensate was prepared from a commercial brand of cigarettes by a machine which simulated human smoking habits, producing three 2-second puffs per minute. The smoke was condensed at −60° C., and after further treatment the average yield of tar was 9·7 g. per 200 cigarettes. This tar, dissolved in acetone solution, was applied to the shaven backs of mice 3 times a week, each dose containing 40 mg. of the tar. Other groups of mice were painted with acetone alone, with croton oil alone, or with croton oil after 7 months of tar treatment. In a few cases denicotinized tar, obtained by washing the tar with 1% hydrochloric acid, was used towards the end of the experiment with a view to reducing its toxic effects.

Of 81 tarred mice, 48 (59%) developed papilloma in a mean time of 56 weeks, and 36 (44%) developed carcinoma in a mean time of 71 weeks, both types of tumour being present in 27 cases. Acetone alone produced no skin lesions; croton oil alone caused roughening and thickening of the epidermis, but no tumours. The results of the application of tar plus croton oil could not be evaluated owing to the high mortality among the animals after 12 months, but no acceleration of tumour induction was noted during the period of observation. Two of the epidermoid carcinomata have been transplanted to several generations of mice. It is concluded that these studies confirm that tobacco tar is a carcinogen for mouse epidermis, but, as the authors stress, it is not known at present which fraction or fractions in tobacco tar are carcinogenic; further studies for the identification of these agents are in progress. *H. G. Crabtree*

## MORBID ANATOMY AND CYTOLOGY

1531. **The Morphogenesis of Old Pulmonary Tuberculous Foci.** (О морфогенезе обострения старых туберкулезных очагов в легких)
I. S. Levenbuk. *Архив Патологии* [*Arkh. Patol.*] **15**, 55–63, Nov.–Dec., 1953. 5 figs., 27 refs.

Pulmonary tuberculous lesions, primary and post-primary, were found at necropsy in 82 out of a series of 96 patients over 20 dying from non-tuberculous causes. Full histological examination was carried out in 65 cases, particular attention being paid to signs of reactivation of the tuberculous lesions. The morphological stages of such reactivation are described, with emphasis on the connexion between the tuberculous focus and the organism as a whole. It is observed that the reactivation of tuberculous disease is frequently overlooked in patients with other serious conditions, and that they constitute therefore a source of unsuspected danger to those around them. *L. Crome*

1532. **Systemic Nodular Panniculitis**
B. Steinberg. *American Journal of Pathology* [*Amer. J. Path.*] **29**, 1059–1081, Nov.–Dec., 1953. 16 figs., 40 refs.

Since 1892 some 46 cases of nodular panniculitis (or Weber–Christian disease as Brill termed it) have been reported in the literature. The present author here describes the clinical and post-mortem findings in 2 further cases seen at Toledo Hospital, Toledo, Ohio.

The disease is shown to be not always confined to the panniculus, but to extend in some cases to the perivisceral fat of several organs as well as that of the omentum and mesentery. The bone marrow may also

be attacked, with consequent abnormalities of the haematopoietic system, and in some cases there is focal necrosis of the spleen and liver. This extension of the disease creates an increased demand for phagocytes, and the lymph nodes, spleen, and liver become enlarged owing to the presence of fat-laden macrophages and to hyperplasia of the reticulo-endothelial elements. The large number of histiocytes present may lead to confusion of the syndrome with lymphoma or possibly leukaemia.

The author suggests that in cases of extensive involvement of tissues the syndrome should be called " systemic nodular panniculitis " (panniculitis, though not strictly accurate, being retained because of its now common usage), and when only the panniculus is affected it should be termed " subcutaneous nodular panniculitis ".

*J. B. Wilson*

1533. **Changes in the Nerve Supply of the Skeletal Muscles in Hypertension.** (К вопросу об изменении нервного аппарата скелетных мышц при гипертонической болезни)

V. B. Zaĭrat'yants. *Архив Патологии* [*Arkh. Patol.*] **15**, 43–49, Nov.–Dec., 1953. 5 figs., 16 refs.

Morphological changes were found on histological examination of the nerve endings of the skeletal muscles of 30 patients dying of hypertension. These are considered to be secondary to vascular dysfunction and non-specific. The " rheumatoid " pains of which certain patients complain may be explained, in some cases, by these lesions.

*L. Crome*

1534. **Pathological Changes in the Blood-vessels and Nerves of the Oesophagus due to Corrosion**

G. Gušić. *Journal of Laryngology and Otology* [*J. Laryng.*] **67**, 745–763, Dec., 1953. 12 figs., 9 refs.

The pathological changes observed in the oesophagus after ingestion of caustic acids or alkalis are described. Acids cause coagulation necrosis, whereas alkalis cause colliquative necrosis. When the acid or alkali is concentrated or when large quantities have been taken oedema is a marked feature, affecting the nerves even in the peri-oesophageal tissues; involvement of the vagus nerve may rapidly lead to death. Vascular thrombosis is also a constant finding. In some cases the lesions in the oesophagus are slight, while those in the larynx, tracheobronchial tree, and stomach are severe; it is suggested that in such cases the functional reactions of the surrounding autonomic nervous system have been abolished or considerably retarded.

Prevention of stenosis is the main object of treatment, and the author discusses experimental work on the use of cortisone for this purpose.

*R. Heptinstall*

1535. **Portal Cirrhosis. Clinical and Pathologic Review of 782 Cases from 16,600 Necropsies**

E. M. Hall, A. Y. Olsen, and F. E. Davis. *American Journal of Pathology* [*Amer. J. Path.*] **29**, 993–1027, Nov.–Dec., 1953. 21 figs., 27 refs.

The authors review the clinical and pathological findings in 782 cases of portal cirrhosis (believed to be the largest series so far considered in one report), selected from the records of some 16,600 necropsies performed at the Los Angeles County Hospital in the period 1933 to 1946. The patients' ages ranged from 10 to 90 years but half were aged between 40 and 60; two-thirds were males, and 80% of the total were heavy drinkers. Histological preparations of liver sections were available in all but 30 of the cases. [Not much that is new emerges from this study.]

Chronic alcoholism was confirmed in most of the cases. Information about the diet, adequate in only 20% of the cases, showed that this was generally deficient and especially poor in protein and vitamins of the B-complex. The incidence of atherosclerosis up to the age of 55 was somewhat lower than that reported in the literature for a comparable group of non-cirrhotic subjects; hypertension was present in only 20% of the patients. The causes of death fell mainly into four categories, as follows: intercurrent acute and chronic infections, 33%; haemorrhage from oesophageal varices, 19% (10% in the subacute group and 25% in the chronic group); hepatic insufficiency, 17%; and cardiac failure, 14%. The authors point out that since 1918 the incidence of death due to cirrhosis has increased from 2% to 5% of deaths from all causes. The case histories showed that many of these patients when first seen had only vague gastrointestinal symptoms, and as liver function tests then gave normal results, the patients were passed from clinic to clinic and received a variety of treatments, including prolonged psychiatric treatment in some cases. It is suggested that more definite information about diet and drinking habits would have pointed to the diagnosis in these cases.

*A. D. Duff*

1536. **Needle Biopsy of the Liver. VIII. Experiences with Hepatic Granulomas**

G. P. Wagoner, A. T. Anton, E. A. Gall, and L. Schiff. *Gastroenterology* [*Gastroenterology*] **25**, 487–494, Dec., 1953. 6 figs., 8 refs.

The wide use of needle biopsy in the diagnosis of suspected hepatic disorders has shown that the liver " is often the incidental seat of lesions which reflect the existence of systemic diseases ". Such lesions frequently take the form of miliary tubercular granulomata which, in the absence of a demonstrable causative agent, are not generally regarded as pathognomonic, having been found in a variety of diseases, including tuberculosis, sarcoidosis, brucellosis, syphilis, tularaemia, and fungus infections. Out of a total of approximately 1,100 needle-biopsy specimens of liver tissue examined at Cincinnati General Hospital, miliary granulomata were encountered in 54, from 38 patients. In 7 instances the tubercles were not present in the initial biopsy but were detected in subsequent specimens. Sections were stained with haematoxylin and eosin, with the periodic acid–Schiff reagent (for the demonstration of fungi), by the Ziehl–Neelsen method for tubercle bacilli, and by the van Gieson and Masson trichrome methods for the evaluation of connective-tissue content. In 3 cases portions of specimens were cultured; in 2 cases the culture was negative, but in the third a growth of *Brucella suis* was obtained. Diagnoses, including tuberculosis, sarcoidosis, syphilis,

lymphopathia venereum, Hodgkin's disease, and brucellosis, were established in 28 cases, whereas in 10 no definitive diagnosis could be made. Active tuberculosis was diagnosed in 13 cases, in 3 of which the disease had not previously been suspected. Similarly in 3 out of 6 cases the diagnosis of sarcoidosis was unsuspected. Syphilitic granulomata were found in the needle-biopsy specimen in 5 cases, the disease being in the secondary stage in 4 and in the tertiary in the fifth; miliary granulomata indistinguishable from those seen in patients with tuberculosis and sarcoidosis were also present in all 5. Granulomatous disease was accompanied by hepatomegaly in 22 and splenomegaly in 11 of the 38 patients. Jaundice was usually absent. Disturbances of liver function were most frequently demonstrated by the zinc sulphate turbidity test and by the serum albumin and globulin levels. *E. Forrai*

1537. **A Histopathological Study of Two Related Types of Hepatitis: Infective Hepatitis and Infectious Mononucleosis.** (Considérations histo-pathologiques sur deux hépatites voisines: l'hépatite infectieuse et la mononucléose infectieuse)
F. BÉNAZET, R. SOHIER, and R. FONTANGES. *Annales de médecine* [*Ann. Méd.*] **54**, 457–482, 1953. 15 figs., 33 refs.

The authors recommend the use of liver biopsy as a diagnostic procedure in distinguishing between clinically atypical cases of infective hepatitis and infectious mononucleosis. The two diseases show similar hepatic lesions in that the connective-tissue reaction consists of a histiocytic and lymphocytic infiltration, usually in relation to the portal tracts. Parenchymal necrosis is characteristic of infective hepatitis, however, although more localized foci of necrosis sometimes occur in infectious mononucleosis. Early biopsy is necessary, as the appearances become less distinctive as the diseases progress.
*G. J. Cunningham*

1538. **The Aetiology of Cytomegalia Infantium.** (Die Ätiologie der Cytomegalia infantium)
W. H. MINDER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 1180–1182, Dec. 5, 1953. 4 figs., 31 refs.

Newborn or very young babies occasionally develop a fatal condition, cytomegalia infantium, characterized by purpuric skin rashes, jaundice, enlargement of the liver and spleen, focal pneumonia, and an erythroblastic or erythro-leucoblastic blood picture; though the condition is suggestive of congenital syphilis, the usual serological tests are negative.

In this paper from the University Pathological Institute, Berne, the histopathological findings are described (and illustrated with photomicrographs) with special reference to a case in a premature child who died 14 days after birth. Post-mortem examination usually shows a chronic inflammatory process, often leading to fibrosis, in the liver, kidney, and pancreas, alveolar inflammation in the lungs, and the presence in these organs, as well as in the thyroid and parotid glands, of characteristic giant cells. These are round or oval cells, 20 to 35 $\mu$ in diameter, with round or oval eccentric nuclei which have a hyperchromatic nuclear membrane, show local chromatinic thickening, and contain large acidophil intranuclear " inclusion bodies ". Between the nuclear membrane and the inclusion body is a clear halo, which stains only faintly or not at all. The protoplasm of many of the cells shows small irregular vacuoles, near which, and particularly clumped in those parts of the cell where the nucleus lies, are finely granular, strongly basophilic structures. In the kidney, similar material appears in the lumen of the convoluted tubules and may be excreted in the urine. These cells have been regarded as protozoa, as cells undergoing degenerative or abnormal developmental changes, or as cells infected with a virus.

The author has examined by electron microscopy pancreatic cells from the fatal case mentioned above and found that between the vacuoles the cytoplasm of the giant cells contained large numbers of spherical particles of fairly uniform diameter (about 100 m$\mu$) connected by a fine protoplasmic network and often clumped in grape-like clusters. The clear zone in the nucleus appeared to consist almost entirely of these granules, but the so-called inclusion bodies were free from them except at their edges. Undamaged cells contained none of these granules, but showed mitochondria and secretion granules which were absent from the giant cells. The author regards the granules in the giant cells as virus bodies, and compares them with those seen in the salivary glands. *C. L. Oakley*

1539. **Myelonecrosis, Extramedullary Myelopoiesis, and Leuko-erythroblastosis. A Mesenchymal Reaction to Injury**
R. J. PEACE. *American Journal of Pathology* [*Amer. J. Path.*] **29**, 1029–1057, Nov.–Dec., 1953. 15 figs., 22 refs.

The author discusses the histogenesis and morphology of the anatomical lesions occurring in the benign myeloproliferative syndromes and describes in detail 4 cases representing four different manifestations of the syndrome seen recently at the M. D. Anderson Hospital for Cancer Research, Houston, Texas.

This disorder is characterized by a leuco-erythroblastic anaemia, and by hepatomegaly and splenomegaly resultant on myeloid metaplasia. The bone marrow passes through phases of necrosis of the haematopoietic cells, reactive hyperplasia, atrophy, fibrosis, and osteogenesis. There is a similar progression of events, ending in fibrosis, in areas of extramedullary haematopoiesis.

Clinically, the liver is moderately enlarged and the spleen markedly so, the patient often presenting with symptoms referable to enlargement of these viscera. Histologically, the cut surfaces of these organs reveal numerous small areas of haematopoiesis; similar areas may be found in lymphoid tissues throughout the body. In the early stages the microscopic changes in the bone marrow are those of marked hyperplasia of all haematopoietic cells, occasionally one or two cell types predominating. In addition, there are numerous foci of necrosis of the immature cells. The cells surrounding these areas of necrosis show a hyperplastic response, and

in turn undergo necrosis. Each succeeding generation of cells is less well differentiated, and eventually the responding cells are mainly haemocytoblasts; there is never any evidence of neoplasia. In the next stage, the marrow undergoes atrophy, with an increase in fat. In addition a ground substance known as myelofibrin is laid down, and this becomes condensed and later ossified. The areas of extramedullary haematopoiesis in the spleen, lymph nodes, liver, and other organs undergo histological changes similar to those in the marrow, except that calcification does not occur. As stated, there is a leucoerythroblastic anaemia, and megakaryocytes and abnormal platelets are present in large numbers in the blood.

Although the cause is not known at present, the author suggests that it is possible that the continued exposure of the mesenchymal-cell system to a variety of cytotoxic factors may produce the successive histological changes seen in this syndrome. *E. G. Rees*

1540. **Systemic Lipid-containing Histiocytoma.** (Das systematische lipidhaltige Histiocytom)
M. LOPEZ. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **324**, 391–408, 1953. 7 figs., 39 refs.

From the Institute of Pathological Anatomy, University of Pisa, 4 cases of primary neoplasm of lymph nodes with systemic spread are described and the histological appearances depicted in photomicrographs. The patients were all men, aged 32, 37, 37, and 48 respectively. In 3 of the cases biopsy specimens were taken from supraclavicular nodes, and in the fourth from inguinal nodes. Clinically, the patients showed a rise of temperature, a neutrophil leucocytosis, and enlargement of the liver and spleen. Three of them died within a year of the onset of illness. Histological examination revealed that in all biopsy preparations the normal structure had been replaced by a system of nodules and strands, mingled with atypical cells of varied size which showed marked vacuolization. The vacuoles contained lipoid material with the following composition: total lipids 32·2%, phosphatides 7·5%, free steroids 4·2%, combined steroids 0·3%, the remainder consisting of neutral fats.

These 4 cases appear to the author sufficiently similar to each other and different from other malignant conditions of the lymphatic system to form a separate disease entity, for which he proposes the name " systemic lipid-containing histiocytoma ". *L. Michaelis*

1541. **The Value of Cytological Examination of the Sputum in the Diagnosis of Carcinoma of the Bronchus**
R. C. JENNINGS and K. M. SHAW. *Thorax* [*Thorax*] 8, 288–294, Dec., 1953. 1 fig., 27 refs.

The authors discuss the value of cytological examination of fresh smears of sputum as an aid in the diagnosis of malignant disease of the lung. A review of the literature shows that the reported percentage of correct diagnoses by cytological examination ranges from 42·8 to 84. The method was introduced at the London Chest Hospital in 1937, and in 1943 became a routine procedure in the examination of all non-tuberculous cases. Various methods of staining have been used by different workers, but the authors have found a wet-film methylene-blue technique, used without glycerin, to be simple, speedy, and constant in result. The method, which is described in detail, has the disadvantage of impermanence owing to precipitation of the stain, and smears must be examined within 4 hours of preparation. It is best to use fresh specimens of sputum when possible, and the selection of a suitable portion of the material is of considerable importance.

The appearance presented by various types of malignant cells is discussed. The most commonly encountered cells in cases of bronchogenic carcinoma are malignant squames; these show considerable variation in size, shape, and staining properties, often a diminished nucleocytoplasmic ratio, the presence of small perinuclear globules, and varying degrees of peripheral progressive keratinization, even to the extent of epithelial pearl formation. Much more rarely found are cells, smaller than the malignant squames, which are arranged in clusters or dense clumps and are to be distinguished from the less darkly stained lymphocytes; these are suggestive of " oat-cell " carcinoma, and their presence in the sputum makes the diagnosis of carcinoma virtually certain. The least commonly found type of cell is one showing massive vacuolation; this is suggestive of adenocarcinoma, but the authors do not believe that this type of tumour can be distinguished cytologically.

Between January, 1950, and November, 1952, 395 known cases of carcinoma of the lung have been examined cytologically; of 286 of these in which at least 6 specimens of sputum were examined, a positive result was obtained in 240 (83·9%). An attempt was made in all cases to distinguish the type of malignant cell present; in 9 cases this was reported as squamous-cell carcinoma but was later shown to be of a non-differentiated type or an adenocarcinoma. The false negative results are analysed; out of 290 cases the cytological examination was negative in 111, undifferentiated or anaplastic carcinoma accounting for 60 of these (54%).

The result of the cytological examination is correlated in tables with the final diagnosis made by histological examination of a biopsy specimen or at necropsy. False positive reports in the literature have ranged between 0·3 and 12·5% in different series; in the present series the figure was 2·5%. False positive results may be due to the presence of atypical macrophages, or of desquamated epithelium from areas of squamous metaplasia in the bronchus, or to the examination of sputum at too short an interval after a preceding bronchoscopy. In 3 of the authors' cases a positive report was correctly based on the presence of malignant cells which were, however, found to have come from a carcinoma of the oesophagus. *Ferdinand Hillman*

1542. **The Relationship of the Weight of the Heart and the Circumference of the Coronary Arteries to Myocardial Infarction and Myocardial Failure**
G. MILLES and W. DALESSANDRO. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 31-37, Jan–Feb., 1954. 3 figs., 10 refs.

# Bacteriology

1543. **Epidemiologic and Immunologic Significance of Age Distribution of Antibody to Antigenic Variants of Influenza Virus**

F. M. DAVENPORT, A. V. HENNESSY, and T. FRANCIS. *Journal of Experimental Medicine* [*J. exp. Med.*] **98**, 641–656, Dec. 1, 1953. 7 figs., 20 refs.

The effects on the antibody content of the population which result from repeated exposure to antigenic variants of influenza viruses have been studied by measuring, with many strains, the antibody content of lots of gamma globulin prepared in different years and the patterns of antibody found in sera collected in one year from various age groups.

In all samples of gamma globulin collected from 1943 through 1951, high levels of antibody were found with strains of Type A and Type B influenza viruses isolated prior to 1941. The highest levels were found in the more recent collections of gamma globulin. Antibodies to A-prime and B strains of 1945 and 1952, were present at low levels in gamma globulin collected prior to the isolation of these viruses. A moderate increase in antibody was observed in the gamma globulin of recent years.

The pattern of distribution of antibody by age found with most A-prime strains in serum pools exhibited high levels in infancy and childhood, but after the age of 20, little or no antibody was detected. With Type A strains antibody was usually not observed until the 11th year of age. Thereafter, high levels were present until age 20, when the amount of antibody declines to a moderate and relatively constant level which persists throughout life. Antibody against swine influenza virus did not become detectable until the 29th year. The intermediate antigenic character of a few A-prime isolates was reflected in the antibody pattern obtained with them. Antibody was not found until age 13 with the Lee (1940) strain of Type B influenza virus, but thereafter the level was high. With the Type B isolates of 1945 and 1952, antibody became measurable at earlier ages.

The present data clearly demonstrate that in the early years of life the range of the antibody spectrum is narrow, and that it becomes progressively broader in later life.

A striking correlation was found between what is known of the periods of prevalence of certain strains of influenza viruses and the age of the people in whom strain-specific antibodies are currently found. It has been observed that the age at which antibodies to certain strains are first detectable has progressively advanced with the passage of time.

From these data the following immunologic thesis is formulated. The antibody which is acquired during the initial infections of childhood is of limited scope and reflects the dominant antigens of the prevailing strains. The immunity conferred by the initial experiences with influenza is also limited. Successive experiences later in life with viruses of related but differing antigenic make-up result in a composite of antibody which is oriented toward a larger number of the common antigens which comprise influenza virus. These experiences confer a broader immunity which limits infection with, and antibody response to, the more recently encountered strains. The antibody-forming mechanisms appear to be oriented by the initial infections of childhood so that exposures later in life to antigenically related strains result in a progressive reinforcement of the primary antibody. The highest cumulative antibody levels detectable in a particular age group tend, therefore, to reflect the dominant antigens of the virus responsible for the childhood infections of that group. Hence the pattern of antibody distribution determined currently in different age groups provides a serologic recapitulation of past infection with antigenic variants of influenza viruses.—[Authors' summary.]

1544. **The Stability of the Viral Potency of Smallpox Vaccine when Prepared in Calf Globulin, Dehydrated, and Stored without Refrigeration**

E. CARDONE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **42**, 693–699, Nov., 1953. 16 refs.

The need for a smallpox vaccine which will not undergo deterioration in tropical and subtropical climates has long been felt. In this paper from the New York City Department of Health Laboratories the author describes how, by combining the protective action of colloids with refrigeration and dehydration, he has obtained a smallpox vaccine which will retain its potency when stored at relatively high temperatures. The vaccine pulp from vaccinated calves was ground and made into a 20% emulsion with calf globulin containing phenol and ether, the final product showing a concentration of 0·5% phenol and 0·8% ether. Volumes of 1 ml. were then placed in glass containers and deep-frozen overnight. The next day they were dehydrated for 2 hours at −75° C. and further dehydrated for 5 hours at room temperature; the containers were then vacuum-sealed.

To test for potency after various conditions of storage, the dry product was emulsified with saline solution and serial dilutions of 1 in 1,000 to 1 in 80,000 were tested on rabbits. After well over 30 days (in some cases 100 days) at 20° to 25° C., dilutions of 1 in 1,000 to 1 in 20,000 gave 100% "takes". The bacterial counts averaged 350 organisms per ml., a figure well below the limit for bacterial contamination specified by the U.S. National Institutes of Health. When the dehydrated vaccine was stored at −28° C. for 423 days and then exposed to temperatures of 20° to 25° C. for 30 days it showed no appreciable deterioration. The author emphasizes the importance of correct technique in dehydration in order to obtain successful results.

*L. J. M. Laurent*

# Pharmacology

1545. **Inhibition of Histamine Death in Pertussis-inoculated Mice by "Dibenzyline", an Adrenergic Blocking Agent**
L. S. KIND. *Journal of Allergy* [*J. Allergy*] **25**, 33–35, Jan., 1954. 5 refs.

"Dibenzyline" (N-phenox*iso*propyl-N-benzyl-β-chloroethylamine) is an adrenergic blocking agent which shows some structural similarity to mepyramine. Mice which had become sensitive to histamine by being previously treated with a vaccine of *Haemophilus pertussis* were used to test the antihistaminic property of the drug. When the animals were given 25 mg. of dibenzyline per kg. body weight they were protected against the effects of adrenaline and also against three $LD_{50}$ doses of histamine. The protective effect against histamine lasted at least 24 hours. *H. Herxheimer*

1546. **Liver Lesions following Intravenous Administration of Polyvinyl Pyrrolidone (PVP)**
E. A. GALL, W. A. ALTEMEIER, L. SCHIFF, D. L. HAMILTON, H. BRAUNSTEIN, J. GIUSEFFI, and D. G. FREIMAN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **23**, 1187–1198, Dec., 1953. 7 figs., 25 refs.

Preliminary observations on the histological changes in the liver after intravenous infusion of the plasma substitute polyvinyl pyrrolidone (PVP) are presented in this paper from the University of Cincinnati. A single intravenous infusion of 1,000 ml. of normal saline containing 3·5 or 4·5% of PVP was given to each of 22 patients with chronic diseases unrelated to disorders of the liver or blood-forming organs. A liver biopsy specimen was taken before the infusion was given, and the histological appearance compared with that of specimens taken from 1½ to 13 months after the infusion. Deposits were found within the Kupffer cells or free in the sinusoids 6 months or more after the infusion, but were rarely seen in the liver in the first 3 months. Minor chronic inflammatory changes were observed around the deposits. The results of histochemical tests suggest that these deposits are related to the fraction of the PVP of higher molecular weight.
*A. Wynn Williams*

1547. **Effects of Papaverine upon Ectopic Ventricular Tachycardia Produced by Myocardial Infarction**
A. S. HARRIS, A. ESTANDÍA, A. BISTENI, and H. T. SMITH. *Circulation* [*Circulation (N.Y.)*] **8**, 874–878, Dec., 1953. 3 figs., 10 refs.

Experiments are reported from Louisiana State University, New Orleans, and Baylor University, Houston, Texas, in which ectopic ventricular tachycardia was induced in dogs by occlusion of the anterior descending coronary artery, a heart rate of 150 to 260 per minute being present after 16 to 20 hours. Doses of papaverine ranging from 3·7 to 8 mg. per kg. body weight injected into those animals with a rate of 160 or less per minute temporarily reduced the frequency to normal, but further administration of the drug was ineffective or caused an increase. In animals with a heart rate of 180 to 270 per minute similar doses of papaverine occasionally caused a transient slight slowing, but sometimes increased the frequency, and in one case caused ventricular fibrillation. It is concluded that papaverine and related vasodilator drugs are dangerous and of little value in the suppression of ectopic ventricular tachycardia, and that such action "is not to be anticipated on a basis of demonstrated vasodilator action even though the best known ectopic suppressor compounds (quinidine, procaine amide, magnesium) have vasodilator properties". *V. J. Woolley*

1548. **Cardiovascular Action of 1:1-Dimethyl-4-phenylpiperazinium Iodide (DMPP). A Ganglion Stimulating Agent Useful in the Diagnosis of Pheochromocytoma**
I. H. PAGE and J. W. MCCUBBIN. *American Journal of Medicine* [*Amer. J. Med.*] **15**, 675–683, Nov., 1953. 4 figs., 17 refs.

The pharmacology of 1:1-dimethyl-4-phenylpiperazinium iodide (DMPP), which was found by Chen, Portman, and Wickel (*J. Pharmacol.*, 1951, **103**, 330) to stimulate autonomic ganglia, has been further studied. The present authors found that in dogs, cats, rabbits, and man DMPP had a more powerful stimulating action and a less powerful paralysing action than nicotine. Its vasopressor action was largely independent of carotid sinus and aortic reflexes, and the drug had little direct action upon the perfused blood vessels of the denervated leg of the dog. The ganglion-stimulating action of DMPP was inhibited by large doses of nicotine and by tetraethylammonium and hexamethonium. Its pressor action was inhibited by adrenergic blocking agents to the same extent as the action of noradrenaline. In dogs with chronic hypertension produced by cutting the carotid sinus and aortic depressor nerves, DMPP acted as in normal dogs, but if the drug was given shortly after division of the nerves the initial rise in blood pressure was followed by a prolonged fall.

An intravenous injection of 1 mg. of DMPP in a patient with phaeochromocytoma caused a rise in blood pressure from 210/135 to 280/200 mm. Hg. A dose of 10 mg. of piperoxan hydrochloride then reduced the blood pressure to 120/70 mm. Hg. When the tumour had been removed 1 mg. of DMPP caused a rise in blood pressure from 130/90 mm. Hg to 145/92 mm. Hg only. The initial bradycardia and other effects of parasympathetic stimulation by DMPP were prevented by administration of atropine, which did not interfere with the test. Administration of DMPP followed by an adrenergic blocking agent may be helpful in the diagnosis of phaeochromocytoma. *L. G. Goodwin*

# Chemotherapy

1549. **Laboratory Aspects of Combined Antibiotic Treatment**

S. D. Elek, G. R. F. Hilson, and P. Jewell. *British Medical Journal* [*Brit. med. J.*] **2**, 1298–1300, Dec. 12, 1953. 2 figs., 25 refs.

Although correlation of the laboratory and clinical findings concerning the action of combined antibiotics is as yet incomplete, there is evidence that two antibiotics used simultaneously may be more effective (synergistic) or less effective (antagonistic) in their action than either antibiotic used alone. This paper from St. George's Hospital, London, records an investigation of the lethal action of combinations of antibiotics, an agar diffusion technique amplified by a simple form of sampling being used. A sterile velvet stamp is pressed on to the surface of a primary agar plate containing both bacteria and antibiotics, and then similarly pressed on to a second plate which contains no antibiotics. Subculture indicates whether the inhibitory effect in the primary plate was bactericidal or bacteriostatic. Altogether 65 strains of common pathogens were tested against 3 pairs of antibiotics. Penicillin with either chloramphenicol or aureomycin generally showed antagonism, whereas streptomycin with chloramphenicol was synergistic, after incubation for 18 to 24 hours at 37° C.

*D. Geraint James*

1550. **Preliminary Observations of the Action of Penicillin on *Treponema pallidum in vivo***

H. E. Morton and W. T. Ford. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 529–535, Nov., 1953. 4 figs., 19 refs.

The authors, writing from the University of Pennsylvania, Philadelphia, recall that when bacteria are exposed to sublethal concentrations of penicillin they swell and elongate to several times their normal length. In the case of the Reiter strain of *Treponema pallidum*, which has a generation time of 7 hours, similar changes are observed within 24 hours; in the case of *T. pallidum*, 90 minutes after injection of 20,000 to 40,000 units of penicillin into patients the proportion of long forms was seen to be increased 3- or 4-fold. As the generation time of *T. pallidum* is 33 hours, this effect must be attributed to the death of the short forms.

The authors carried out similar studies on 3 patients with untreated syphilis. After the presence of *T. pallidum* had been confirmed the patients were given 40,000 units of penicillin, and at 2-hourly intervals thereafter dark-ground specimens were prepared and examined, the length of 100 treponemes being measured on each occasion with an eye-piece micrometer. In the first case no change was detected in the over-all length of the organisms, which became scanty after 8 hours and had disappeared after 10 hours. In the second case observation had to be discontinued after 6 hours because the organisms had become so scarce. The last case was followed for 8 hours, after which no more treponemes could be found. The authors also grew the Reiter and the Nichols strains of *Treponema pallidum in vitro*. The organisms retained their normal morphology when grown in the presence of up to 0·002 unit of penicillin per ml. of medium, but became elongated when exposed to 0·004 unit per ml.; no visible growth was obtained with a concentration of 0·039 unit per ml. The results of the study *in vitro* are presented in graphs in which the percentage frequency is plotted against the length of the organisms.

The failure to detect treponemes in 8 to 10 hours after the start of penicillin therapy accorded well with the findings reported by other workers. In cases of gonorrhoea, however, some authors have reported negative culture 3·7 hours after the beginning of treatment; the generation time of gonococci is 30 minutes. It is concluded that the rapid disappearance of treponemes from lesions must be due to lysis, numerous observations being quoted from the literature in corroboration of this postulate, and it is considered that it cannot be due to phagocytosis or adherence to erythrocytes (as has been suggested), since in that event antibody, complement, and other serum components would not be changed so rapidly.

*Ferdinand Hillman*

1551. **Activity of Erythromycin against *Staphylococcus aureus***

D. Hobson. *British Medical Journal* [*Brit. med. J.*] **1**, 236–239, Jan. 30, 1954. 4 figs., 17 refs.

Erythromycin, an antibiotic produced by *Streptomyces erythreus*, is active against a wide range of Gram-positive organisms and also against the neisseriae, *Haemophilus influenzae*, *H. pertussis*, and certain strains of *Brucella*. It can be given orally and is of low toxicity; it is excreted in satisfactory concentration in the urine, but is not found in the cerebrospinal fluid. Erythromycin is likely to be of particular value against staphylococci resistant to other antibiotics, and its activity against pathogenic staphylococci has therefore been the subject of investigations carried out at St. Mary's Hospital, London. The strains used included isolates from infections, nasal and oral flora, and stock cultures, and their sensitivity was determined to serial dilutions of crystalline erythromycin (potency 915 μg. per mg.), 5-hour broth cultures being used for inoculation. Plates were used for routine sensitivity tests, and could be kept for 2 weeks in the refrigerator without loss of erythromycin potency. Resistant variants were obtained by serial subculture at 48 hours on 10% blood–agar plates or ditch plates incorporating erythromycin.

Sensitivity was unaffected by inoculum size, continued incubation, variation of the temperature of incubation between 26° and 40° C., or the addition of 25% serum.

A total of 213 coagulase-positive, mannitol-fermenting strains of staphylococcus were tested, of which all were sensitive to 0·5 μg. and 26% sensitive to 0·25 μg. of erythromycin per ml. There was no difference in sensitivity between any of 33 strains of *Staph. aureus* of known phage-type drawn from each of the 3 main groups, while 47 strains with various degrees of resistance to penicillin, streptomycin, chloramphenicol, and oxytetracycline (" terramycin ") were all sensitive to 0·25 to 0·5 μg. of erythromycin per ml. Daily viable counts of staphylococci in broth cultures containing different concentrations of erythromycin showed that while no growth was obtained after 24 hours with samples from the tubes containing 4 and 1 μg. per ml., sterilization was not complete after 72 hours in 0·5 μg. per ml.; with lower concentrations the count remained stationary for a period and then began to rise, while with 0·1 μg. per ml. the count was similar to that of the control culture after 24 hours.

The development of resistance in 14 strains of staphylococcus was examined by the serial-subculture method and appeared to follow the " stepwise " pattern found with penicillin; resistance developed rapidly in all 14 strains, 2 of which became resistant to 80 μg. per ml. after only 5 subcultures, all having originally been sensitive to 0·25 to 0·5 μg. per ml. The colonial appearance, mannitol fermentation, coagulase production, and phage pattern of the resistant organisms were the same as those of their parents, the only change observed being that the growth of the resistant organisms, measured turbidimetrically, was less active. There was no evidence of any erythromycinase production, nor were erythromycin-dependent variants isolated. None of the resistant organisms was cross-resistant to penicillin, streptomycin, chloramphenicol, or oxytetracycline, but there was cross-resistance to " magnamycin " (carbomycin).

*Malcolm Woodbine*

1552. **Ototoxicity of a Mixture of Streptomycin and Dihydrostreptomycin. A Preliminary Report**
E. G. Sita Lumsden and R. J. Powell. *Tubercle* [*Tubercle* (*Lond.*)] **34**, 324–330, Dec., 1953. 16 refs.

The effect on vestibular function and hearing of streptomycin sulphate was compared with that of a mixture of equal parts of the sulphates of streptomycin and dihydrostreptomycin (" ambistryn "). One group of 20 patients received 1 g. daily of streptomycin and a second group of 20 patients received 1 g. daily of ambistryn; both groups received in addition 12 g. of PAS a day, treatment being continued for 12 weeks. The therapeutic effect of the antibiotics was similar in both groups. Vestibular disturbance was more common among the patients given streptomycin, 12 of whom had vertigo, alone or with ataxia, or a non-reacting labyrinth. Only 5 of the patients receiving ambistryn developed vestibular symptoms, and these were mild. Hearing loss was observed in 3 of the patients receiving ambistryn. Three patients who had severe vestibular symptoms while receiving 1 g. of streptomycin daily were able to tolerate 1 g. of ambistryn without serious effect. The authors state that the indications for the use of ambistryn are similar to those for streptomycin alone, but that ambistryn should not be given by intrathecal injection. It is particularly suitable for prolonged administration at the rate of 1 g. daily, especially to patients over the age of 50, in whom vestibular disturbance after streptomycin therapy is relatively more frequent, and to patients who are, or become, intolerant of streptomycin and require further treatment.

*Derek R. Wood*

1553. **The Mode of Action of Proguanil and Related Antimalarial Drugs**
J. F. Ryley. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **8**, 424–430, Dec., 1953. 1 fig., 16 refs.

An investigation was carried out into the antimalarial activity of proguanil, its dichloro analogue (5943), their respective triazine metabolites, and pyrimethamine (to which the metabolites bear a marked structural resemblance), and into the relation between antimalarial activity and interference by substances active in the pteroylglutamic acid system. Two methods were used: (1) employing a culture of *Lactobacillus casei* in a medium containing varying amounts of pteroylglutamic acid (PtG); and (2) employing chick erythrocytes parasitized with *Plasmodium gallinaceum* and suspended in a chick-serum medium at 38° C. for 24 or 40 hours [the culture method is novel; for its details the original should be consulted]. All 5 compounds inhibited the growth of *L. casei*, the triazines and pyrimethamine being considerably more active than proguanil and 5943. The action of the more toxic substances was competitively reversed by added PtG, but no reversal occurred with proguanil or 5943. In the absence of PtG competitive reversal occurred with the addition of thymine in the case of the triazines and pyrimethamine, but not in the case of proguanil or 5943. With the triazines and pyrimethamine one molecule of PtG reversed the toxic action of several thousand molecules of drug, but a more nearly equimolecular relationship existed between these drugs and thymine. It is therefore argued that the drugs exert their antimalarial effect by interfering with reactions involving thymine or its derivatives, and not by antagonism of PtG.

Morphological changes occurring in *P. gallinaceum in vivo* after proguanil treatment of the host are described, and suggest that the drug acts by inhibiting chromatin synthesis and nuclear division. Similar changes were produced in *P. gallinaceum in vitro* by proguanil (1 mg. per litre), 5943 (0·5 mg. per litre), by their respective triazine metabolites (0·01 mg. and 0·001 mg. per litre), and by pyrimethamine (0·005 mg. per litre), while approximately 10 times these concentrations reduced culture viability by 90%. The antimalarial activity of proguanil and of the triazine metabolite of 5943 *in vitro* could not be reversed by the addition of PtG, citrovorum factor, adenosine, or a mixture of adenine, guanine, and thymine. It is suggested that the plasmodia may possibly be unable to use PtG but require a " higher form " of folic acid, and rather than use free purines or pyrimidines in the synthesis of nucleic acids, prefer to utilize the corresponding nucleosides or nucleotides.

Proguanil-resistant *P. gallinaceum* in culture proved to be insusceptible to the action of all 5 drugs except at concentrations much higher than those producing inhibitory effects on a normal strain. The morphological effects produced by these higher doses did not suggest the typical interference with chromatin synthesis.

*I. M. Rollo*

1554. **The Action of Isoniazid–Streptomycin and Isoniazid–Dihydrostreptomycin Mixtures on Tubercle Bacilli**
A. BERCZELLER, G. FRANK, and C. J. PAPA. *Quarterly Bulletin of Sea View Hospital* [*Quart. Bull. Sea View Hosp.*] **14**, 174–185, Oct., 1953. 15 refs.

Mixtures of isoniazid and dihydrostreptomycin showed synergism against *Mycobacterium tuberculosis in vitro* in contrast to mixtures of isoniazid and streptomycin, which showed antagonism. This difference may be explained by the condensation of the hydrazine radical of isoniazid and the carbonyl radical of streptomycin to form the *iso*nicotinyl hydrazine of streptomycin, whereas in dihydrostreptomycin the carbonyl group has been converted to the non-reactive carbinol group, so that no such condensation takes place. *A. W. H. Foxell*

1555. **Estimation of the Antileukemic Potency of the Antimetabolite Aminopterin, Administered Alone and in Combination with Citrovorum Factor or Folic Acid**
A. GOLDIN, N. MANTEL, S. W. GREENHOUSE, J. M. VENDITTI, and S. R. HUMPHREYS. *Cancer Research* [*Cancer Res.*] **13**, 843–850, Dec., 1953. 4 figs., 17 refs.

It has previously been shown that either the citrovorum factor (C.F.) or folic acid can reduce the lethal toxicity of aminopterin for mice, and that the effectiveness of this inhibition is determined by the dose levels and relative times of administration of these substances. As folic acid and C.F. also interfere with the tumour-inhibiting effects of aminopterin, the quantitative aspects of this action were studied at the National Cancer Institute, Bethesda, Maryland, with the results here described.

The relative effectiveness of four types of treatment in prolonging the survival time of mice inoculated with lymphoid leukaemia L 1210 were compared. Aminopterin was administered (*a*) alone, (*b*) concomitantly with folic acid or C.F., or (*c*) one hour after the administration of folic acid. The aminopterin and folic acid were given in a 2% solution and the C.F. in a 0·5% solution of sodium bicarbonate by subcutaneous injection in single doses 3 days after the tumour implantation, each in a volume corresponding to 1% of the animal's body weight. This procedure allowed a distinction to be made between animals dying from aminopterin toxicity (6 to 9 days after tumour implantation), and those dying from the tumour itself (between 14 and 16 days). The results are analysed statistically.

In all four types of treatment increasing doses of aminopterin caused a corresponding increase both in mortality from the drug and in survival time in animals which died of the leukaemia. For any given dose of aminopterin, C.F. (or folic acid injected one hour earlier) caused a fall in mortality from the drug, but also lowered the time of survival of aminopterin-treated mice, that is, the antimetabolite was more effective when given alone than when given in conjunction with C.F. or after the administration of folic acid. When folic acid was injected simultaneously with aminopterin it had no effect on the toxicity or antileukaemic action of this antimetabolite. *H. G. Crabtree*

1556. **Synergistic Inhibitory Action of A-methopterin and a Diaminopyrimidine upon Leukemia L 1210 in Mice**
E. M. NADEL and J. GREENBERG. *Cancer Research* [*Cancer Res.*] **13**, 865–868, Dec., 1953. 1 fig., 19 refs.

The folic acid analogue a-methopterin and an antimalarial drug, 2:4-diamino-5-(3′:4′-dichlorophenyl)-6-methylpyrimidine, were tested alone and in combination for their effect on tumour size and period of survival of 751 mice inoculated with the transmissible leukaemia L1210 in a study carried out at the National Cancer Institute, Bethesda, Maryland. The drugs were first given 3 days after tumour inoculation, and then on every other day.

The pyrimidine was toxic at a dose level of 10 mg. per kg. body weight, but checked the rate of tumour growth and promoted longer survival. At half this dose or less, however, although tumour growth was retarded, the drug had no effect in prolonging survival time. A-methopterin, in doses of 2·5 mg. per kg., also prolonged survival time and slowed the rate of tumour growth, but was ineffective at the lower dose of 1·5 mg. per kg. body weight.

When high doses of the two drugs were administered in combination their effect was less than additive, but combined low doses proved to be synergistic, the antileukaemic action being more than additive; for example, a-methopterin in a dose of 1·5 mg. per kg. together with 2·5 mg. of the pyrimidine per kg. caused a notable retardation of tumour growth and increased the average survival time by 92%, though each drug in these doses was ineffective when given alone. *H. G. Crabtree*

1557. **Azaserine, a New Tumour-inhibitory Substance. Studies with Crocker Mouse Sarcoma 180**
C. C. STOCK, D. A. CLARKE, H. C. REILLY, C. P. RHOADS, and S. M. BUCKLEY. *Nature* [*Nature (Lond.)*] **173**, 71–72, Jan. 9, 1954. 3 refs.

A preliminary account is given of the investigation, at the Sloan–Kettering Institute for Cancer Research, New York, of the tumour-inhibitory properties of crude filtrates of a broth culture of a *Streptomyces*, and of the isolation of azaserine, a crystalline antibiotic substance highly active against the Crocker mouse sarcoma 180. Azaserine is a substituted L-serine, and was found to be effective in inhibiting tumour growth when given intraperitoneally in amounts as low as 1 to 2 mg. per kg. body weight daily for one week.

The authors state that "it is not clear yet whether azaserine will be useful against human cancer; but, in view of its structure and its effects in various biological systems, the compound should prove a helpful tool in biochemical studies". A full account of these effects is to be published elsewhere. *Donald Crowther*

# Infectious Diseases

1558. **A Skin Test for Mumps using Cerebrospinal Fluid from Cases of Mumps Meningitis**
C. CHOREMIS, C. DANELATOU, C. DENTAKI, and D. GOUTTAS. *Lancet* [*Lancet*] **2**, 1126–1128, Nov. 28, 1953. 11 refs.

Enders (*Ann. intern. Med.*, 1943, **18**, 1015) and Habel (*Publ. Hlth Rep. (Wash.)*, 1945, **60**, 201) showed that patients convalescent from mumps develop skin hypersensitivity to the virus; the former used as antigen a suspension of infected monkey parotid gland and the latter a suspension of egg-yolk from infected chick embryos. In view of the fact that the cerebrospinal fluid (C.S.F.) of patients with mumps meningoencephalitis contains the virus, the present authors, at the Children's Clinic, Athens University, used a preparation of the C.S.F. as antigen. Samples of C.S.F. obtained from patients with mumps meningoencephalitis on the 5th, 10th, and 15th days of the disease were inactivated at 65° C. for 20 minutes and centrifuged at 2,000 r.p.m. for 30 minutes, the sediment then being diluted and injected intradermally into patients with mumps or a history of mumps and into controls. A positive reaction consisted in an area of redness measuring 3 to 10 mm. and a zone of infiltration of 2 to 5 mm. There was no reaction in patients with mumps to injection of C.S.F. obtained on the 10th and 15th days, but all 34 patients with mumps or convalescent from the disease gave a positive reaction to the C.S.F. obtained on the 5th day in a dilution of 1 in 10. There was no reaction in 28 controls. When this skin test was performed on children at an orphanage shortly after an outbreak of mumps a positive reaction was obtained in 90% of those who had had the disease in the previous 6 months, and in 65% of those who had had it in the previous 2 years. The reaction was also positive in 10% of the children without a history of mumps.

No reaction was obtained in patients with mumps to C.S.F. taken in the active phase of poliomyelitis, infectious mononucleosis, lymphocytic choriomeningitis, and chickenpox, nor did patients suffering from these diseases react to C.S.F. from patients with mumps meningoencephalitis. *L. J. M. Laurent*

1559. **Human Infection with Viruses of the Colombia SK Group.** [In English]
J. D. VERLINDE and H. A. E. VAN TONGEREN. *Archiv für die gesamte Virusforschung* [*Arch. ges. Virusforsch.*] **5**, 217–227, 1953. 8 figs., 16 refs.

At the Netherlands Institute for Preventive Medicine, Leiden, a search was made for Columbia SK virus in several hundred specimens of stools, throat washings, and cerebrospinal fluid from suspected cases of poliomyelitis, encephalomyelitis, aseptic meningitis, and epidemic pleurodynia. The stools (in 20% suspension) and throat washings (undiluted) were cleared by centrifugation and injected, with 500 units of penicillin and 2·5 mg. of streptomycin, intraperitoneally or subcutaneously into suckling mice or intracerebrally into older mice or monkeys. Cerebrospinal fluid was similarly treated, but no antibiotic was added. Virus isolated by this method was considered to belong to the Columbia SK group if it possessed a high mouse-infectivity titre and if infected mouse-brain suspensions agglutinated sheep's erythrocytes or human O cells and were neutralized (or haemagglutination inhibited) by Columbia SK hyperimmune serum prepared in monkeys.

A virus showing these characteristics was isolated from 3 children aged 1 to 2 years diagnosed clinically as suffering from aseptic meningitis, paralytic poliomyelitis, and encephalomyelitis respectively. Animals (from the same batches as those used for isolation) inoculated with other human material showed no signs of infection. A rise in antibody level was observed in 2 of the patients. It is therefore concluded that the viruses were not laboratory contaminants or the result of activation of latent animal viruses, and that infection by viruses of the Columbia SK group may occur in man. *R. Hare*

1560. **Risk of Death from Asphyxiation in Measles Encephalitis**
P. BENDZ and C.-G. ENGSTRÖM. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **86**, 772–776, Dec., 1953. 1 fig., 9 refs.

The authors describe 3 cases of measles encephalitis which were successfully treated at the Stockholm Hospital for Infectious Diseases although the patients were admitted in a moribund condition. They emphasize the danger of asphyxia from retention of mucous secretion in the respiratory tract, and suggest that this is a fundamental contributory cause of the repeated convulsions, which decrease or cease with adequate aeration.

The treatment given consisted in (*a*) postural drainage in the face-down position; (*b*) artificial respiration with concurrent aspiration of mucus from the nasopharynx; and (*c*) administration of oxygen through a nasopharyngeal catheter. The authors state that artificial respiration should not be given with the patient in the dorsal position because of the risk of asphyxiation from persistence of mucus in the bronchi.

[The commonly-used Nelson bed is suitable for postural drainage in such cases.] *D. Geraint James*

1561. **Appendicitis in the Course of Measles**
W. H. GALLOWAY. *British Medical Journal* [*Brit. med. J.*] **2**, 1412–1414, Dec. 26, 1953. 13 refs.

Acute appendicitis in association with measles in childhood is not, in the author's view, a fortuitous occurrence, 7 cases having been seen at the City Hospital, Aberdeen, over a period of 18 months. In all the cases abdominal symptoms were present for 12 to 72 hours

before the rash appeared. It is suggested that enlargement of lymphoid tissue in the submucosa of the appendix, which is known to occur in measles, causes ischaemia of the appendix and interferes with the flow of lymph, leading in turn to necrosis and bacterial invasion. Histological examination of the appendix removed during the prodromal stage of measles in one case showed an intense lymphoid reaction and the presence of multinucleated cells and a type of giant cell.

From an analysis of the 42 cases in the literature and the 7 reported here it was found that symptoms of appendicitis developed during the prodromal stage in 19 cases, the eruptive period in 17, and the immediate convalescent period in 13.

It is concluded [rightly] that appendicitis should be suspected when abdominal pain develops during measles and that because of the danger of perforation, operation should not be delayed. *R. S. Illingworth*

1562. **Clinical, Prophylactic, and Therapeutic Aspects of Botkin's Disease [Infective Hepatitis] in Hot Climates.** (Клиника, профилактика и лечение болезни Боткина в условиях жаркого климата)
E. M. Tareev. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 3–11, Dec., 1953.

Infective hepatitis predominates in hot climates over other forms of liver disease since, like all intestinal infections, it is easily disseminated in such conditions. The inoculated or parenteral form is also widely known, being often transmitted in injections against malaria or (in some areas) yellow fever. The disease cannot be regarded as affecting the liver only, and still less as being confined to the epithelial cells of that organ It is rather a disease of the hepato-lieno-medullary systems. The frequent disturbances of the globulin and monocyte and plasmocyte content of the blood confirm this view, while in children the lymphoid tissue is often involved. Besides the general disturbance of the digestive tract there is also interruption of the metabolic and neuro-endocrine links and excessive activity of certain steroids and hormones. Leporski has studied the effects upon the cerebral cortex, but less attention has been paid to lesions of the pyramidal and extrapyramidal systems and the vegetative nervous system, although the hepato-lenticular syndrome has been recognized in acute forms of the disease.

The causative organism is a virus, and the disease is transmissible in the prodromal stage. It is therefore of importance to recognize the clinical symptoms and isolate the patient as early as possible. An influenza-like or dyspeptic syndrome, with anorexia, pyrexia, arthralgia, urticaria, splenomegaly, and enlarged liver, should suggest infective hepatitis. There may be also, especially in children, enlargement of the cervical and submaxillary lymph nodes, a polymorphous rash, catarrhal pharyngitis, and a vesicular eruption on the mucous membrane of the soft palate, which is often slightly icteric. At this stage liver function tests may already indicate hepatic involvement and bilirubinaemia may be present.

The non-icteric form of the disease is usually abortive or mild, but may progress to a serious or even fatal termination, with acute or subacute hepatic necrosis or cirrhosis. Its diagnosis is often difficult; complement-fixation tests are occasionally of value in early diagnosis. Hepatolenticular degeneration has been observed in some cases as a sequel of non-icteric hepatitis. The author believes that 20% of non-icteric cases develop cirrhosis, and that 75% of all cases of cirrhosis result from infective hepatitis. In addition, there is a chronic form which is characterized by repeated recrudescences. The parenteral form is identical with the naturally acquired form, differing only in its prolonged incubation period and its greater severity and mortality, especially in children. Transmission of the infection is often by prophylactic injection against measles. Whether the difference in incubation period and severity depends upon the site of entry of the infection or, as immunological evidence suggests, on variations in the strains of the virus, is uncertain.

The possibility that primary cancer of the liver may result from hepatic changes arising from viral hepatitis as a late sequel cannot be excluded. It has been observed that in Samarkand, where the incidence of cirrhosis is high, primary cancer of the liver is also common.

There is no specific cure for infective hepatitis; treatment is mainly symptomatic, consisting chiefly in rest and diet. High-protein diets and the administration of amino-acids (casein hydrolysate, methionine, choline, or lecithine) have received much attention, but the author pronounces no final judgment as to their value. He considers that it is unsound to regard viral hepatitis as basically a nutritional deficiency disease, for it is primarily a virus infection. The use of penicillin or other antibiotics in uncomplicated cases, however, cannot be recommended without reserve. The chief aims of treatment are to shorten the period of jaundice and to prevent the supervention of the chronic stage. The latter aim has not been achieved by the various methods of treatment which have so far been attempted. The main lines of prophylactic treatment are the early isolation of patients, particularly in the prodromal stage, and prevention of spread of the disease by faecal or manual contamination. The scrupulous disinfection of syringes used for injections, blood transfusions, and for obtaining blood samples is essential for the prevention of parenteral hepatitis. Methods of sterilization adequate to kill pyogenic organisms may not suffice to destroy the resistant virus of infective hepatitis. The control of flies is also of the highest importance, especially in hot climates. Specific immunization with gamma globulin cannot at present be widely carried out; it is indicated mainly in circumscribed communities or in the case of persons exposed to special risk of infection.

*L. Firman-Edwards*

1563. **The Recognition of Whooping-cough**
D. Court, H. Jackson, and G. Knox. *Lancet* [*Lancet*] **2**, 1057–1060, Nov. 21, 1953. 2 figs., 1 ref.

The onset and course of whooping-cough, as seen in 388 out of a total of 906 children observed throughout the first 5 years of life, are described in detail. The authors distinguish whooping-cough from the other respiratory conditions, especially bronchitis, commonly

seen in this age group. It is defined as " any illness in which the child develops a rapid spasmodic choking cough, generally associated at some stage with vomiting and less often with whooping, and lasting for a month or more ".

Of the 388 children, 97 had whooping-cough in the first year of life; the 3 deaths in the series occurred in infants under one year. The most frequent symptoms in infancy were cough, vomiting, and whooping or choking. It is pointed out that, unlike measles, whooping-cough was continuously present in the community throughout the 5-year period, without epidemic peaks. The value of a history of contact is emphasized; when there was contact within the family circle the infectivity rate was high, 8 out of every 10 susceptible children contracting whooping-cough. The authors conclude that although the severity of the disease varies considerably, there is a constant pattern of illness in the majority of cases, " and whooping-cough can be strongly suspected in many of these in the first ten days ".

*T. Anderson*

1564. **Antibiotic and Antigenic Therapy of Brucellosis with Special Reference to the Chronic Disease. A Report on 421 Cases**

H. J. HARRIS. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] 3, 982–989, Oct., 1953. 13 refs.

The author has collected 421 presumed or confirmed cases of brucellosis during the 6-year period 1945–51. The age of the patients varied between 5 and 89 and in the majority of cases the disease was chronic, but in 15 it was acute and 28 were seen during exacerbation. The various methods of diagnosis are discussed. In the acute febrile illness agglutinins in high titre or positive blood cultures of *Brucella* are found in the majority of patients. In the chronic illness (defined as of more than 3 months' duration) this is rarely so except during exacerbation, and presumptive diagnosis depends on additional specific, though less reliable, tests. These include complement-fixation tests, skin tests, and determination of the opsonocytophagic reaction.

Various antibiotics known to be effective against *Brucella* infection were employed by the author. In the acute febrile cases, streptomycin and dihydrostreptomycin administered parenterally (with sulphadiazine orally), and aureomycin, chloramphenicol, oxytetracycline, and erythromycin orally, were given as a routine, either singly or in various combinations. Antigens were not employed in this stage. In chronic cases, treatment was usually initiated with *Brucella* antigens (killed *Brucella abortus* organisms, Castaneda's M.B.P., or brucellar bacterial antigen complexes) in sub-tolerance doses as a therapeutic trial. The antibiotics were employed whenever recovery was not complete, often being given alternately with, or at the same time as, additional courses of antigen. A detailed account of dosage schedules is given. In small doses (1 g. per day), all the antibiotics mentioned were well tolerated. In larger doses (2 g. per day), oxytetracycline was better tolerated than aureomycin, and chloramphenicol intermediately so. The side-effects and sequelae, which included avitaminosis and moniliasis (usually self-limiting), are discussed, as well as methods for their prevention and treatment.

On the whole, the results of treatment were satisfactory, the author attributing this, in part at least, to the fact that repeated courses of antibiotics and/or *Brucella* antigen were usually employed and the patients kept under observation for long periods, so that more treatment could be given promptly when required; another reason was that the less virulent strains of *Br. abortus* predominated. Streptomycin and dihydrostreptomycin, especially in the chronic disease, were not quite so useful as the other antibiotics under trial, but *Brucella* antigens played an important role when given alone or in conjunction with the antibiotics. *J. V. Armstrong*

1565. **Family Studies on Brucellosis**

W. W. SPINK. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 128–133, Feb., 1954. 25 refs

1566. **Some Clinical Observations and Findings in Penicillin Treatment Given in the Scarlet Fever Epidemic in Zagreb from 1949–1951.** [In English]

B. MRAVUNAC, B. BEZJAK, and P. LJUBIBRATIĆ. *Acta medica Scandinavica* [*Acta med. scand.*] **147**, 253–264, Dec. 11, 1953. 7 figs., 17 refs.

The clinical features of an extensive outbreak of scarlet fever which occurred in Zagreb during a 15-month period in 1949–51 are described. The outbreak followed a familiar pattern, but was of special interest because the type of scarlet fever, though mild (with only 2 deaths out of 3,172 cases), was intermediate between the classic type common 25 years ago and the abortive type seen in Western Europe and North America today. The epidemic thus provided a better opportunity for studying the therapeutic value of penicillin than is generally possible nowadays.

The incidence was highest in the period July, 1950, to January, 1951, with a marked peak in November, 1950. Clinically the disease was " mild " in 45·5%, " moderately severe " in 52·5%, " toxic " in 1·5%, and " septic " in 0·5%. Complications occurred in 26·1% of the cases, mainly in the second, third, and fourth weeks of the illness, and it is admitted that many were due to cross-infection in hospital, there being a shortage of isolation facilities at the peak of the epidemic. The most frequen complications were lymphadenitis and angina. Nephritis accounted for 1·9% and otitis media for 1·5% of the complications, while relapse occurred in 1% of the cases. [These are not high figures in the circumstances.]

In treatment, a single dose of 300,000 units of procaine penicillin in oil was given daily for 5 to 7 days. This had no effect on the pyrexia, the average duration of which was 3·6 days after the start of penicillin therapy, but throat swabs became negative for β-haemolytic streptococci within 48 hours, and the incidence of complications fell from 29·1% in untreated cases to 20·3% in treated cases. Later, when isolation became possible, the incidence of complications in treated cases fell to 9·0%.

*H. Stanley Banks*

# Tuberculosis

1567. **Filtrate of Tuberculous Pus as a Therapeutic Agent**
M. C. WILKINSON, J. B. PENFOLD, and E. WILDER *Tubercle* [*Tubercle* (*Lond.*)] **34**, 288–296, Nov., 1953. 5 refs.

At Black Notley Hospital, Essex, 51 patients with tuberculosis were treated with subcutaneous injections of a bacteria-free filtrate of tuberculous pus. Most of the patients had skeletal tuberculosis, and in all cases progress had previously been unsatisfactory and the prognosis poor; no control series was available. The dose was 0·25 to 0·5 ml. for children and 0·5 to 1·0 ml. for adults, given with an equal volume of saline thrice weekly. Only one reaction due to hypersensitivity was seen. Beneficial effects possibly attributable to the treatment were seen in 31 cases, including: (1) recalcification of carious bone so that mobility was preserved in pseudarthroses; (2) absorption of pus or inhibition of pus formation; and (3) healing of sinuses.

In experiments on guinea-pigs injected with tubercle bacilli there was a significant reduction in the severity of lesions at the inoculation site and in the lungs in treated animals, but not in the case of lesions of other organs.

*D. Weitzman*

1568. **Preliminary Clinical Trials of a New Antimycobacterial Drug: *para*-Aminosalicylic Acid Hydrazide.**
(Prime esperienze cliniche con un nuovo antimicobatterico: l'idrazide dell'acido para-amino-salicilico)
M. REALE, A. GARAVENTA, and M. GHIONE. *Minerva medica* [*Minerva med.* (*Torino*)] **1**, 138–145, Jan. 20, 1954. 12 figs., 9 refs.

1569. **The Treatment of Tuberculous Pericarditis**
E. M. GOYETTE, E. L. OVERHOLT, and E. RAPAPORT. *Circulation* [*Circulation* (*N.Y.*)] **9**, 17–21, Jan., 1954. 6 figs., 9 refs.

The authors report from Fitzsimons Army Hospital, Denver, Colorado, good results in the treatment of 27 patients with tuberculous pericarditis by chemotherapy, first with streptomycin alone, later with the addition of PAS, and in recent cases with streptomycin and isoniazid; they emphasize the need for prolonged treatment, which means at least a year in hospital, to ensure the best results.

At a follow-up examination made after periods of 6 months to 3 years, 21 of the patients were completely asymptomatic. Of the remaining 6, one died in the initial stages from widespread dissemination of the tuberculosis and the other 5 developed constrictive pericarditis, one of whom also died. In this last group there had been some delay in every case in starting chemotherapeutic treatment, and the authors believe that this and inadequate dosage are the main causes of failure of treatment.

Diagnosis of the condition is often difficult, and air replacement of the effusion or even pericardial biopsy may be necessary, but if in doubt it is reasonable to give a course of streptomycin and isoniazid. Persistence of signs of congestion in spite of adequate medical treatment is evidence of constriction, and surgery should be undertaken even if the disease is still active.

*A. Paton*

## RESPIRATORY TUBERCULOSIS

1570. **Late Results of Treatment of the Solitary Dense Tuberculous Pulmonary Focus (Tuberculoma) without Resection or Chemotherapy**
R. S. MITCHELL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 471–478, Sept., 1953. 6 figs., 10 refs.

The literature on the treatment of the solitary, dense, circumscribed tuberculous focus, the tuberculoma, is discussed. Good results have been reported in over 75% of cases treated medically and followed up for 6 months to 15 years. Early results of resection have been favourable, but some time must elapse before the late results can be evaluated.

Examination of the clinical records of all patients admitted to the Trudeau Sanatorium, New York, between January, 1930, and December, 1949, revealed 39 solitary, dense tuberculous foci. The progress of the patients after discharge from the hospital was traced, the follow-up period varying between 4 and 22 years. Treatment consisted in modified bed rest and minor surgical measures only (2 patients had a very short course of chemotherapy). The focus was in the infraclavicular region in 22 cases and in the apex in 7; foci were present in both lungs in one case only.

The results of this follow-up investigation indicated that when medical treatment only was given the disease progressed in one out of every 4 cases. The author therefore regards resection as desirable [but most of the patients had not received any drug treatment and, moreover, the relapses were not serious.]

*T. Marmion*

1571. **Control Study of Isoniazid: Factors Influencing the Response of Pulmonary Tuberculosis to Chemotherapy**
UNITED STATES PUBLIC HEALTH SERVICE. *Diseases of the Chest* [*Dis. Chest*] **24**, 361–377, Oct., 1953. 4 figs.

In April, 1952, the U.S. Public Health Service invited physicians in 22 tuberculosis hospitals to undertake a large-scale trial of isoniazid. The hospitals were scattered throughout the United States, and the 583 patients concerned were considered to represent a cross-section of patients in civilian tuberculosis hospitals in that country. By a system of random selection three comparable groups were formed and given isoniazid alone, isoniazid plus streptomycin, and streptomycin plus PAS

respectively, in addition to whatever other treatment the patient's condition required. Each patient underwent a 64-week initial period of observation, a 40-week period of chemotherapy, and a 24-week period of observation after stopping chemotherapy. The present report presents an analysis of the radiological changes occurring during chemotherapy, films being taken at 4-week intervals.

No change was noted in slightly more than one-fifth of all cases, there being about the same proportion in each treatment group, and deterioration occurred in 3 to 6%. Of those showing improvement, the isoniazid–streptomycin group showed a slight superiority over the other groups throughout treatment. No difference was apparent between the groups treated with streptomycin and PAS and with isoniazid alone. The differences in response within each group were much greater than between the groups. Older patients showed less improvement generally than the younger. Of patients under 45 the proportion with improved *x*-ray findings was greater among whites than non-whites, but the reverse was the case in those over 45. Significant improvement was noted in almost the same proportion of minimal, moderately advanced, and far advanced cases. Of those patients with moderately and far advanced disease, a greater proportion improved when the disease was confined to one lung than when both were involved. A much higher proportion of those who had been in hospital for less than one year before chemotherapy improved than of those who had been in hospital for longer periods. *T. M. Pollock*

1572. **The Treatment of Pulmonary Tuberculosis with Combinations of Antibiotics and Chemotherapeutic Agents, with Special Reference to Dihydrostreptomycin, " Paratebin ", and Isoniazid.** (Die kombinierte antibiotische und Chemotherapie der Lungentuberkulose unter besonderer Berücksichtigung von Dihydrostreptomycin, Paratebin und Isoniaziden)

H. NIEMSCH and W. SITT. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **110**, 329–350, 1953. 13 figs., bibliography.

The authors report the results of clinical trials with dihydrostreptomycin, isoniazid, and " paratebin " given separately, and with the last two in combination, in the treatment of pulmonary tuberculosis. According to the authors, one ampoule of paratebin contains 1 g. of dihydrostreptomycin and 400,000 units of oxyprocain-penicillin. A total of 653 cases were treated (including 139 control cases treated conservatively, without chemotherapy), and the proportions in which both radiological and clinical improvement was obtained were as follows: (1) 139 controls, 10·8%; (2) 49 cases treated with dihydrostreptomycin alone, 32·7%; (3) 116 cases treated with paratebin alone, 41·6%; (4) 71 cases treated with paratebin and isoniazid, 49·3%; and (5) 278 cases treated with isoniazid alone, 18·4%. [For the dosages used and other clinical details the original paper should be consulted.] After an analysis of these results from all points of view the conclusion is reached that paratebin in combination with isoniazid is the treatment of choice for exudative and fibrotic forms of pulmonary tuberculosis with or without cavities. This combination has the advantage that the total dose of each drug can be reduced, toxic side-effects avoided, and the development of drug resistance prevented. *Franz Heimann*

1573. **Isonicotinic Acid Hydrazide and *para*-Aminosalicylic Acid in the Treatment of Pulmonary Tuberculosis**

C. S. BREATHNACH. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] **6**, 433–444, Nov., 1953. 1 fig., 42 refs.

The combination of isoniazid and PAS is eminently suitable for the treatment of pulmonary tuberculosis in patients who have become permanently sensitive to streptomycin or in whom the organism has become streptomycin-resistant; it is also useful in cases in which surgery is contemplated, although streptomycin should be used as a cover for the operation. The effects of this treatment on a total of 36 patients with bilateral tuberculous infiltration of the lungs and a positive sputum were investigated at the Rialto Hospital, Dublin. In a few cases " postured recumbency " and pneumoperitoneum were also used. The daily dose of isoniazid was 6 mg. per kg. body weight, and of PAS 600 mg. per kg. Treatment lasted for 3 months and was followed by 3 months' observation. All but one of the patients improved and in 90% of them the improvement was more than slight; only 10 patients failed to gain in weight (owing in some cases to pneumoperitoneum), and the erythrocyte sedimentation rate fell appreciably in nearly all cases. Radiological appearances in one case remained unchanged, in 12 showed either " slight " or " moderate " improvement, and in 22 showed " considerable " improvement. Clinical deterioration occurred in 2 patients, of whom one died. In 4 cases in which it was possible to assess sensitivity to isoniazid no impairment was found.

The author considers that the over-all results justify the combined use of these two drugs; they are easier to administer than streptomycin and toxic symptoms are few. In view of the close relationship between bacillary resistance and clinical improvement it is recommended that repeated sensitivity tests be carried out in all cases. *Paul B. Woolley*

1574. **The Intravenous Administration of Dihydrostreptomycin.** (Administration intraveineuse de dihydrostreptomycine)

J. BEERENS and P. KLUYSKENS. *Acta tuberculosea Belgica* [*Acta tuberc. belg.*] **44**, 457–463, Dec., 1953. 4 refs.

Previous experimental work has shown that cysteine derivatives will protect the 8th nerve nuclei from the toxic effects of dihydrostreptomycin without interfering with the bacteriostatic action of the antibiotic. The authors have made use of this fact in giving large doses of dihydrostreptomycin intravenously, with the object of attaining high bacteriostatic blood levels of the drug and thus increasing the likelihood of diffusion into lesions, and possibly also preventing the development of drug resistance. [No blood drug levels were actually determined in this series.]

At the Hôpital Civil, Ghent, 13 patients with pulmonary tuberculosis were treated with 3 g. of dihydrostreptomycin every third day, to a total of 30 to 54 g. The drug was dissolved in 500 ml. of saline solution and infused intravenously over a period of 2 to 2¼ hours; this was followed by the intravenous injection of 200 mg. of a cysteine derivative, " becaptan ". (The sclerosing action of the latter led to its being given orally later in the series.) On the whole the cysteine derivative was well tolerated; some patients experienced headache and flushing, and one became syncopal after intravenous injection of the derivative but was able to tolerate it when given by mouth. Periodic tests of auditory and vestibular function showed no evidence of deterioration of hearing. The patients were given PAS on the days between injection, and the course was followed by treatment with isoniazid. Improvement was noted in all 13 patients, some of whom had previously not responded to streptomycin given intramuscularly.

*D. Weitzman*

1575. **Clinical Observations on Viomycin Sulphate in the Treatment of Tuberculosis**

R. L. Hackney, E. Q. King, E. E. Marshall, K. A. Harden, and H. M. Payne. *Diseases of the Chest* [*Dis. Chest*] **24**, 591–600, Dec., 1953. 6 figs., 7 refs.

The authors have used viomycin sulphate in a dose of 2 g. twice weekly combined with 12 g. of PAS daily in the treatment, at Freedmen's Hospital, Washington, D.C., of 35 patients suffering from pulmonary tuberculosis. The results were considered to be somewhat less good than those obtained in a control series of 24 patients treated with streptomycin and PAS. Nevertheless the authors conclude that viomycin is of value in the treatment of pulmonary tuberculosis, particularly in patients in whom the causal organism has become resistant to streptomycin. Toxic effects were not marked, and although tinnitus occurred in a number of cases, damage to the auditory nerve was rare. *R. H. J. Fanthorpe*

1576. **Dramamine (Dimenhydrinate) as an Adjunct to PAS (*para*-Aminosalicylic Acid) in the Treatment of Pulmonary Tuberculosis**

L. I. Leonard. *Diseases of the Chest* [*Dis. Chest*] **24**, 601–607, Dec., 1953. 16 refs.

In a series of 108 tuberculous patients under treatment at the Tuberculosis Hospital, Lantana, Florida, with acid PAS and sodium bicarbonate, 17 were not able to tolerate the PAS owing to severe gastro-intestinal symptoms, diarrhoea, and loss of weight. Unwilling to abandon the use of PAS in these cases, the authors tried the effect of " dramamine " (dimenhydrinate) in a dosage of 50 mg. 3 times per day. This was found to be effective in controlling the symptoms of intolerance to PAS in 14 of the 17 patients, and enabled them to complete the course of treatment. The drug was found to be much less effective, however, in controlling symptoms of intolerance in patients treated with the sodium salt of PAS. The main side-effect of dimenhydrinate was drowsiness, which most of the patients, however, found not unpleasant. *R. H. J. Fanthorpe*

1577. **An Investigation of the Recent Increase in the Rate of Notification of Respiratory Tuberculosis**

C. R. Lowe and J. E. Geddes. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **7**, 227–230, Oct., 1953. 1 fig., 2 refs.

In England and Wales in recent years the number of notifications of respiratory tuberculosis has risen while the number of deaths from this disease has fallen. In an attempt to determine whether this was due to increased incidence of tuberculosis or to improved methods of case-finding the authors examined the records at the Birmingham Chest Clinic, where over 90% of the patients notified in the area are examined.

It was found that the increase beween 1940 and 1952 in the number of notifications from all sources was not due to an increase in tuberculosis morbidity but to the introduction of mass miniature radiography (nearly 25% of all new cases being diagnosed by this means) and, about equally, to the increase in the number of contacts and suspects examined. In the same period the proportion of patients with notifiable lesions discovered among contacts and suspects examined at the clinic fell from 17 to 9% and from 6 to 2% respectively, suggesting that the incidence of respiratory tuberculosis is actually falling. The increase in the number of notifications is attributed to more effective methods of case-finding.

*J. Lorber*

1578. **Results following Pulmonary Resection of Tuberculous Disease with Special Reference to Localized Necrotic Lesions**

J. H. Forsee, C. W. Tempel, and E. L. Scott. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 463–470, Sept., 1953. 1 fig., 2 refs.

Between January, 1947, and May, 1952, at the Fitzsimons Army Hospital, Denver, Colorado, 221 patients underwent resection for localized tuberculous lesions of the lung, defined as lesions involving only one lobe and limited to an area not exceeding the extent of pulmonary parenchyma above the level of the second costochondral junction. In this paper the results of a follow-up investigation are reported. The lesions were classified according to the radiological and pathological appearances as cavitary, encapsulated, multiple nodular, or diffuse. Though the type of operation differed with the form of disease the complication rate did not vary significantly. Wedge resection was carried out in 68 cases, segmental resection in 38, and lobectomy in 115. The operation of choice for cavitary disease was lobectomy and for tuberculoma, wedge resection. In just half the cases resection was associated with thoracoplasty. There were complications in the immediate postoperative period in only 5 cases (bronchopleural fistulae in 2; chest-wall sinus in 1; empyema in 1; and spread of the disease in 1). Late complications were reactivation of the pulmonary disease in 5 cases (on the side of the resection in 4 cases) and non-pulmonary tuberculous adenitis in 2. At the time the report was published 207 of the patients were well, 127 of them being in full- or part-time employment.

[There are two aspects of this work which merit consideration. Chemotherapy was given for at least 4

months after operation; this may account for the low postoperative complication rate. There was only one early postoperative death in the series, this being due to a transfusion reaction; there were no late deaths due to the operation or to tuberculosis. A resection mortality of 0·5% reflects very favourably upon surgical skill. In similar series recently reported mortality has varied from 1% to 25%, 2% being commonly recorded in smaller series. The authors' results are the more remarkable in that many of the operations, especially in the earlier part of the period, must have been performed without the aid of anti-tuberculosis drugs and with unproven techniques.] *T. Marmion*

1579. **Tuberculosis of the Pectoral Segment.** (Tuberculose do segmento peitoral)
J. Pinto Nunes, A. Pinheiro, and M. Neves Dos Santos. *Gazeta médica portuguesa* [*Gaz. méd. port.*] **6**, 660–680, 1953. 39 figs, 19 refs.

Tuberculosis of the anterior segment of the upper lobe of the lung is rare compared with that affecting the posterior and apical segments, the percentages in this study of 60 cases being 15·18 and 84·82 respectively. The authors believe that the lesion arises from bronchial involvement and that proof of this is furnished by ordinary radiography, tomography, and bronchoscopy. The lesion is most commonly on the right side (86·6% of cases). Tuberculosis of the anterior segmental bronchus may arise either from reactivation of a primary complex in the nodes or from exogenous infection. Of the 60 cases which formed the material for this study, the lesions were accompanied by cavitation in 50% and some degree of atelectasis in 25%. Tomography was carried out on 40 patients, and in 28 cases tuberculous endobronchitis was demonstrated; the authors regard tomography as greatly superior to bronchoscopy as a means of diagnosis. The prognosis appears to be good, only 7 cases showing deterioration.

Pneumothorax was induced on 19 patients and 16 of these improved; in 12 cases segmental atelectasis occurred after the induction, but the authors do not regard segmental bronchial involvement as a contraindication to pneumothorax. *Paul B. Woolley*

## TUBERCULOUS MENINGITIS

1580. **The Mantoux Test in Tuberculous Meningitis**
L. M. Taylor, H. V. Smith, and R. L. Vollum. *Tubercle* [*Tubercle* (*Lond.*)] **34**, 296–300, Nov., 1953. 18 refs.

While studying the use of intrathecal tuberculin as an adjuvant to streptomycin in the treatment of tuberculous meningitis at the Radcliffe Infirmary, Oxford, the authors observed a rough correlation between the tuberculin sensitivity of the skin and the meninges. They therefore determined the skin sensitivity to tuberculin in every case, on admission and at intervals during treatment, and here present their findings in 63 cases in patients of all ages and at all stages of the disease. The Mantoux tests were made with old tuberculin (O.T.) and were read after 48 hours, the presence of oedema and induration [diameter not stated] being accepted as a positive result. The largest dose given was 0·1 ml. of 1/100 O.T.

Among their many findings was that in a high proportion (39%) of the cases there was no reaction to 1/1000 O.T. and they are therefore of the opinion that the patch test is of no value in the diagnosis of this disease. If the initial Mantoux reaction was negative the prognosis was generally poorer than the average, but a negative reaction at the outset did not preclude eventual recovery, which occurred in 4 out of 14 such cases. In 5 cases an initially negative reaction beame positive before death. Under streptomycin treatment the intensity of the Mantoux reaction tended to increase, and it became easier to provoke the focal meningeal reaction with intrathecal tuberculin, the authors finding it difficult to provoke these reactions in individuals whose skin sensitivity to tuberculin was such that they reacted only to 0·1 ml. of 1/100 O.T. *J. E. M. Whitehead*

1581. **Tuberculous Meningitis. Combined Therapy with Cortisone and Antimicrobial Agents**
S. J. Shane and C. Riley. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 829–834, Nov. 19, 1953. 5 figs., 14 refs.

The preliminary results obtained with cortisone combined with streptomycin and PAS in the treatment of 7 cases of tuberculous meningitis at the Point Edward Hospital, Sydney, Nova Scotia, are reported. The general scheme of treatment consisted in the daily administration of 200 to 300 mg. of cortisone by mouth, 1 g. of streptomycin intramuscularly, and PAS by mouth up to limit of tolerance. In one case isoniazid replaced streptomycin. Cortisone was given in this dosage until there was decided improvement in the clinical condition and in the laboratory findings, when it was gradually withdrawn. Treatment with streptomycin and PAS was continued for 3 to 6 months after the withdrawal of cortisone.

Of the 7 patients, 3 were adults aged 28 to 36, and 4 were children aged 9 months to 12 years. There were 2 deaths in the series—an 18-month-old child and a man of 31, both of whom were moribund on admission. In the other 5 cases there was "early and dramatic" clinical improvement, attributed to the addition of cortisone to the treatment regimen. In one case there was resolution of an established subarachnoid block and in another an incipient block disappeared. One patient had residual deafness, "probably the result of streptomycin therapy". Intrathecal administration of streptomycin was not necessary except in one case, and then for a short period only. Post-mortem examination in the 2 fatal cases revealed exudate at the base of the brain and miliary tubercles elsewhere.

In an addendum, the authors refer to a later series of 4 cases of tuberculous meningitis similarly treated, in which there was early clinical and laboratory improvement. They emphasize that this total of 11 cases is too small and the follow-up period too short for definite conclusions to be drawn, but they regard the short-term results as encouraging. *Charles McNeil*

# Venereal Diseases

1582. ***Trichomonas vaginalis* Infections in the Male**
F. LANCELEY. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **29**, 213–217, Dec., 1953. 11 refs.

The author has investigated the incidence of *Trichomonas vaginalis* in 735 men attenting venereal disease clinics in Manchester. The methods of examination are described. The organism was found in 2 (0·7%) of 285 cases of gonorrhoea, in 18 (5·8%) of 310 cases of non-gonococcal urethritis, and in 5 (12·5%) of 40 cases of balanitis. In a group of 100 " normal " men, only 1 case of *T. vaginalis* was found. In the cases of non-gonococcal urethritis, *T. vaginalis* was recovered from the urethra alone in 10 cases, the urethra and prostatic secretion in 6, and the urethra, prostate, and subpreputial sac in 2.

The conclusion is reached that, judged by the short course of the infestation (1 to 34 days) and the tendency to spontaneous cure, there seems to be no evidence of chronic infestation. The occurrence of trichomonads in the urethra and prostatic secretion without signs or symptoms suggests that the organism is not essentially pathogenic, but may become so in the presence of other, at present unknown, factors. The most important factor in attaining cure of urethral discharge of long duration appears to be avoidance of re-infection by abstaining from sexual intercourse. Sulphonamides or antibiotics were administered in most cases. The author comments on the high incidence of *T. vaginalis* among the cases of balanitis, and remarks that the low over-all incidence, compared with that reported by other workers, was probably due to the strict criteria adopted for identification of the organism. *V. E. Lloyd*

1583. **Unitary *v.* Plural Conception of Antilipid Antibody in Syphilitic Serum**
A. K. MITRA, S. K. BISWAS, S. SEN, and N. C. BHATTACHARJEE. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **29**, 228–230, Dec., 1953. 15 refs.

In this paper from the Government Venereal Diseases Research Department, West Bengal, the authors describe experiments made to test the suggestion of Rein and Kostant (*Arch. Derm. Syph.* (*Chicago*), 1949, **60**, 217) that the complement-fixing antibodies in syphilitic serum differ from the flocculating antibodies in that the former are univalent and the latter bivalent. The higher incidence of positive results of complement-fixation tests in infants born of syphilitic mothers was attributed to the passage of the smaller univalent antibody molecule through the placenta.

Portions of serologically positive syphilitic serum were allowed to react with Kahn antigen, V.D.R.L. cardiolipin antigen, and Wassermann antigen. [The " M.R.C. No. 14 " method used presumably refers to the Harrison–Wyler Wassermann technique.] After standing overnight at 6° to 8° C. the mixtures were examined for complement-fixing activity: (*a*) without further treatment; (*b*) after centrifuging, the supernatant being examined with and without the addition of W.R. antigen; and (*c*) after the mixtures had been passed through a Seitz filter and the filtrates tested for complement-fixing activity alone and with added Wassermann antigen. Control tests on non-syphilitic sera were also carried out. In the tests on positive sera, complete fixation of 3 M.H.D. and 5 M.H.D. of complement was obtained with the serum–antigen–saline mixtures (*a* above), partial fixation with the supernatants (*b*) both with and without added Wassermann antigen, and no fixation with the Seitz-filtered mixtures (*c*).

After the Wassermann reaction had been carried out the serum–antigen–complement–erythrocyte mixtures were centrifuged and the supernatant fluids subjected to the Kahn and V.D.R.L. slide tests. Reactivity with the flocculation tests was found to be abolished or greatly reduced in all cases.

From these results the authors conclude that since treatment of syphilitic serum with either a complement-fixation antigen or a flocculation antigen removes all complement-fixing and flocculating antilipoid antibody from the serum, the two antibodies are identical. They suggest that the finding of a higher incidence of positive results with complement-fixation tests than with flocculation tests in infants born of syphilitic mothers can be explained by the higher sensitivity of the former test.

[The Wassermann antigen in the absorption experiments was used at a titre of 1 in 1·1 of saline and not, as in the Harrison–Wyler technique, at a titre of 1 in 14.] *A. E. Wilkinson*

1584. **The Significance of the Presence of the Antiprotein Antibody in the Serum in Latent Syphilis.** (Sul valore della presenza dell'anticorpo antiproteico (TL) nel siero del sifilitico latente)
V. A. PUCCINELLI. *Giornale italiano di dermatologia e sifilologia* [*G. ital. Derm. Sif.*] **94**, 369–378, Sept.–Oct., 1953.

The author presents, from the University Dermosyphilitic Clinic, Sassari, Sardinia, a critical study of the significance of the persistence of an antiprotein antibody titre (" TL ") in the serum of otherwise seronegative syphilitic patients. This phenomenon occurs mainly in cases which have been late or insufficiently treated, and a return to seropositivity can often be induced in them experimentally by suitable treponemal stimulation. The persistence of a TL titre is thus evidence against complete cure having been achieved.

Out of 100 such cases, observed for periods of 18 months to 6 years, 6 are described in detail to illustrate the above statement. The primary infection had been contracted at least 10 years previously, and during the period of observation the patients had all had an acute flare-up with return of seropositivity, and in all cases

clinical improvement was obtained by means of anti-syphilitic treatment. In 3 cases there were cardiac symptoms, such as infarction or angina, and in one case the patient gave birth to an obviously congenitally syphilitic child. Apart from the finding of a positive TL titre these patients would by the usual criteria have been considered as completely cured.

The author postulates that in these cases just enough treponemes survive to give rise to the antiprotein antibody, but not enough to stimulate the formation of the antipolysaccharide and antilipoid antibody. He suggests that, as it is not practicable to treat a patient until TL negativity is obtained, patients with a positive TL titre should be kept under close observation and further treatment given (1) if the TL titre rises, or (2) if the antilipoid or antipolysaccharide antibody is again detected.

*Ferdinand Hillman*

1585. **Differences in the Risk of Infection in Children of Syphilitic Mothers.** (Über Unterschiede in der Syphilisgefährdung der Kinder luetischer Mütter)
G. GUMPESBERGER. *Österreichische Zeitschrift für Kinderheilkunde und Kinderfürsorge* [*Öst. Z. Kinderheilk.*] 9, 209–224, 1954. 27 refs.

From a study carried out at the Venereal Diseases Clinic, University of Vienna, of 921 living infants born to syphilitic mothers the author concludes that the risk of congenital syphilis is greatest if the mother contracted the infection during pregnancy and remained untreated. In 25 such cases, 14 of the infants were syphilitic. The risk of congenital syphilis was very slight if the mother received adequate treatment before the birth, and it mattered little whether this was given during pregnancy or before it. From 224 syphilitic mothers who received penicillin as the main therapeutic agent either before or during pregnancy, all the infants born were free of syphilis.

The results were slightly less favourable when treatment was with arsenic and bismuth; 5 out of 118 mothers thus treated had syphilitic infants. But even after " inadequate " treatment with arsenic and bismuth (defined as less than 2 courses of 5 g. each of neoarsphenamine), the risk to the infant was substantially less than in the untreated group. In a group of 116 inadequately treated mothers, 16 pregnancies resulted in syphilitic infants. It was also shown that if the serological reaction of the mother at term was negative or weakly positive the infant was rarely infected.

*G. W. Csonka*

1586. **Familial Investigation in Syphilis. A Review of 670 Families in whom the Original Patient Suffered from a Form of Syphilis other than the Acquired Contagious Type**
W. V. MACFARLANE. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **29**, 203–209, Dec., 1953. 4 refs.

While the literature contains a number of reports on the results of investigation of the familial contacts of patients with acquired contagious syphilis, little has been published about the familial contacts of patients suffering from congenital, latent, or late acquired syphilis. In this paper from the Newcastle General Hospital, Newcastle upon Tyne, the author describes the results of an examination of 1,575 contacts of 542 patients with acquired non-contagious syphilis and 128 with congenital syphilis. Originally 2,284 contacts were traced, but 218 had died and difficulties were encountered in securing the attendance for examination of 491. Of the 1,575 contacts, 328 were found to be infected, the incidence in contacts of patients with acquired non-contagious syphilis (1,231) being 13% (164 cases) and in contacts of patients with congenital syphilis (344) being 48% (164 cases). Among the 328 contacts there were 15 with cardiovascular and 26 with neurological lesions.

The author states that the chief difficulties encountered in carrying out this investigation were: (1) the patient's fear of discovery; (2) prevalence of latent syphilis in the original patients, resulting in contacts failing to realize the gravity of the disease; and (3) difficulty in persuading the original patient to arrange for examination of contacts at a venereal diseases clinic. [The methods of overcoming these are discussed at length in this valuable article.]

*V. E. Lloyd*

1587. **Primary Pustular Gonorrhea of the Skin**
J. L. BYERS and D. F. BRADLEY. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **68**, 503–505, Nov., 1953. 1 fig., 4 refs.

1588. **Complement-fixation Test for Lymphogranuloma Venereum in Non-specific Urethritis**
A. D. MACRAE and R. R. WILLCOX. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **29**, 231–235, Dec., 1953. 3 refs.

To determine whether there was any association between the lymphogranuloma-venereum–psittacosis group of viruses and non-specific urethritis, the authors, working at the Virus Reference Laboratory, St. Mary's Hospital, London, carried out 410 complement-fixation tests for lymphogranuloma venereum in 127 males with non-specific urethritis (4 of whom also had epididymitis, 1 prostatitis, and 7 Reiter's syndrome), in 14 female consorts, and in a control group of 132 patients attending venereal disease clinics with miscellaneous complaints. The technique used was that described by Macrae (*Brit. J. vener. Dis.*, 1951, **27**, 183; *Abstracts of World Medicine*, 1952, **11**, 282), and a titre of over 1 in 40 was held to indicate infection with one of the lymphogranuloma–psittacosis group of viruses.

It was found that 6 of the patients with urethritis had titres of 1 in 40 or over; 2 of these were among the 4 patients whose urethritis was complicated by epididymitis. No positive reactions were found among the patients with Reiter's syndrome. But 3 patients in the control group also gave titres of more than 1 in 40. Serial tests were also carried out on 52 of the urethritic patients, but they showed no significant change in titre.

The authors conclude that their study failed to establish any significant relationship between non-specific urethritis and the viruses of the lymphogranuloma-venereum–psittacosis group.

*A. E. Wilkinson*

# Tropical Medicine

1589. **Comparison of Diaminodiphenylsulfone and Thiosemicarbazone in the Treatment of Lepromatous Leprosy. Clinical and Bacteriological Evaluation in Sixty Hospitalized Patients**
F. SAGHER and N. BRAND. *International Journal of Leprosy* [*Int. J. Leprosy*] **21**, 161–167, April–June, 1953. 15 refs.

The results obtained with diaminodiphenylsulphone (DDS), and with thiosemicarbazone in 60 cases of lepromatous leprosy treated at the Hospital for Hansen's Disease, Jerusalem, are compared. DDS was given orally to 27 patients for 24 months; the daily dose was increased from 100 mg. to 300 mg. over a period of 3 weeks and then maintained at 300 mg. daily, one week's rest being given after every 3 weeks' treatment. Two forms of thiosemicarbazone were used, the *para*-acetylaminobenzaldehyde form (thiacetazone) and the *para*-ethylsulphenylbenzaldehyde form: they were given orally to 21 patients for 6 to 16 months, the dose being gradually increased from 25 to 150 mg. daily, every fourth week being without treatment. One group of 12 patients who had been given DDS were transferred after 2 years to thiosemicarbazone therapy, their condition having become stationary after an initial improvement.

Toxic reactions, chiefly transient headache and epigastric distress, occurred with both drugs, and 5 patients (not included in the total) were unable to receive either treatment owing to violent lepra reactions. Of the 60 patients, more than one-half developed lesions like those of erythema nodosum; it was possible in all but 2 cases to continue treatment, but in a few cases temporary interruption or reduction of dosage was required. Anaemia occurred, but was controlled with iron, liver, and vitamins. No changes in the leucocyte count were noted.

From the clinical and bacteriological results, which are summarized in two tables, both drugs appeared to be effective, thiosemicarbazone probably more so than DDS. The former drug caused further clinical and bacteriological improvement in most of the 12 cases which had become stationary under treatment with DDS.

*W. H. Horner Andrews*

1590. **The Pilomotor Response to Intradermally Injected Nicotine: an Aid in Excluding the Diagnosis of Leprosy**
H. L. ARNOLD. *International Journal of Leprosy* [*Int. J. Leprosy*] **21**, 169–172, April–June, 1953. 2 figs., 6 refs.

In 8 cases of leprosy the normal pilomotor and sudomotor responses to an intradermal injection of 0·1 ml. of 1:100,000 solution of nicotine picrate appeared to be consistently abolished in and near affected areas of skin. In normal subjects, however, the responses were not always seen, and were often absent from the face. On the other hand responses were usually obtained in lesions due to conditions other than leprosy, such as vitiligo and seborrhoeic dermatitis. It is therefore concluded that "a normal pilomotor (gooseflesh) response to an intradermal injection of 1:100,000 nicotine picrate solution strongly suggests that the lesion within which it occurs is not due to leprosy", but that "failure of the response to occur is of uncertain significance".

*W. H. Horner Andrews*

1591. **The Effect of BCG in Lepromatous Cases of Leprosy**
J. LOWE and F. MCNULTY. *International Journal of Leprosy* [*Int. J. Leprosy*] **21**, 173–177, April–June, 1953. 2 refs.

An intradermal injection of 0·1 g. of B.C.G. was given to 104 Nigerian patients with lepromatous leprosy who had shown no reaction to tuberculin or lepromin. On retesting after 2 months, definite sensitivity to tuberculin was now noted in 88 cases and to lepromin in 12 cases, sensitivity to both being present in 11. On retesting with lepromin after one year, sensitivity was shown to have developed in many further cases, but a positive reaction was obtained in only 3 out of 10 of the cases in which the result at 2 months had been positive, the sensitivity developed being evidently only temporary in the rest. There was no indication that the conversion of the lepromin reaction from negative to positive by injection of B.C.G. improves the prognosis; nor did it appear that the severity of the leprosy infection, its duration before beginning treatment, the duration or form of treatment, or the bacteriological status at the time of inoculation with B.C.G. greatly influenced the conversion rate.

*W. H. Horner Andrews*

1592. **The Histoplasmin Reaction in Leprosy Patients**
S. J. BUENO DE MESQUITA and W. A. COLLIER. *International Journal of Leprosy* [*Int. J. Leprosy*] **21**, 179–185 April–June, 1953. 2 refs.

The effect of leprosy on the histoplasmin reaction was studied in Surinam, Dutch Guiana, where a high proportion of the population is histoplasmin positive.

The test consisted in the intradermal injection of 0·1 ml. of a 1:1,000 dilution of a histoplasmin preparation, the reaction being read 48 hours later and being considered positive if there was an area of notable induration more than 4 or 5 mm. in diameter. It was applied to 675 patients with leprosy, representing 92% of the patients in three separate establishments, and to 932 non-leprous persons. The incidence of positive reactions to histoplasmin amongst adult male and female patients with leprosy was virtually identical, being 25·3% and 26·1% respectively, while the figures for boys and girls under 15 years old were 13·5% and 17·8% respectively. In the non-leprous group 45·4% of the adults gave positive reactions (men 55·5%, women 41·7%), while the incidence among non-leprous children was virtually the same as

among the leprous children. Those patients with the least advanced lepromatous lesions ($L_1$) had the lowest incidence of positive histoplasmin reactions (15·9%), the figures for cases of $L_2$ and $L_3$ lepromatous leprosy and of tuberculoid leprosy being 25·5%, 33·0%, and 31·1% respectively. The possible reasons for this reduction of hypersensitivity to histoplasmin in the presence of active leprosy are discussed, the most likely explanation being thought to be that there is "a kind of antagonism" between the leprosy bacillus and *Histoplasma*.

*W. H. Horner Andrews*

1593. **BCG in the Prophylaxis of Leprosy. A Preliminary Report**

N. DE SOUZA CAMPOS. *International Journal of Leprosy* [*Int. J. Leprosy*] **21**, 307–312, July–Sept., 1953. 11 refs.

Between February and December, 1952, 1,658 persons in contact with leprosy, attending for examination at the central dispensary of the Department of Leprosy Prophylaxis of the State of São Paulo, Brazil, were vaccinated with B.C.G. vaccine, receiving 200 mg. by mouth weekly for 3 weeks: in the same period 3,329 contacts were examined but not vaccinated. At the time of reporting, 10 cases of leprosy had been noted in the vaccinated group (an incidence of 0·6%) and 179 cases in the non-vaccinated group (an incidence of 5·4%).

In the vaccinated group the leprosy was tuberculoid in all instances, being reactional in 5, of the childhood nodular form in 4, and circinate in one. In contrast, 47 (26·3%) of the cases in non-vaccinated contacts were of the lepromatous form, 84 (46·9%) of undifferentiated form, and only 48 (26·9%) of the tuberculoid type. It is concluded that B.C.G. vaccination clearly has a protective effect against leprosy.

[These findings will doubtless be of very great interest to those conducting international work on B.C.G. and leprosy control.] *R. R. Willcox*

1594. **The Value of Lepromin Reaction in the Diagnosis of the Clinical Forms of Leprosy**

S. SCHUJMAN. *International Journal of Leprosy* [*Int. J. Leprosy*] **21**, 313–322, July–Sept., 1953. 4 figs., 2 refs.

The author stresses the importance, in assessing the results of the lepromin test, of making a reading after 21 days as well as after 2 days, a positive 21-day reaction (Mitsuda phenomenon) sometimes occurring after the early result (Fernandez reaction) has been negative, but never the reverse. In his opinion the immunological findings, and particularly the Mitsuda reaction, are of great value in the classification of indeterminate cases and cases without cutaneous manifestations. In lepromatous leprosy the lepromin reaction is consistently negative, whereas the clinical, bacteriological, and histological characteristics may undergo modification from time to time. In tuberculoid leprosy the lesions are more stable, although clinical modifications do occur slowly and are accompanied by corresponding histological changes; the lepromin reaction, however, always remains positive, with slight oscillations in the degree of intensity but without ever becoming negative. In the author's experience indeterminate cases with a negative lepromin reaction, both early and late, usually develop into the lepromatous type, whereas he has never known a strongly lepromin-positive case to become lepromin negative or to be transformed into the lepromatous type; however, the number of cases observed has been too small to permit definite conclusions to be drawn. It is in indeterminate cases with a weakly positive lepromin reaction that the greatest difficulty of interpretation is encountered, but study of the immunological evolution of such cases by means of 3-monthly tests may be helpful.

*R. R. Willcox*

1595. **Fumagillin in Amoebiasis**

R. ELSDON-DEW, A. J. WILMOT, and T. G. ARMSTRONG. *Lancet* [*Lancet*] **2**, 1180–1181, Dec. 5, 1953. 1 fig., 9 refs.

Fumagillin has been found to have a lethal effect on *Entamoeba histolytica in vitro*, but no effect on bacterial flora. In the investigation reported in this paper from Durban fumagillin was tried in the treatment of acute amoebic dysentery in the African male. A dose of 40 mg. of fumagillin was given daily for 10 days to 7 patients and a dose of 200 mg. daily for 10 days to 48 patients. In the smaller dosage fumagillin proved completely ineffective. The results of treatment with the larger dosage were classified as "successful" in 28 of the 48 patients, "probable failure" in 10, and "absolute failure" in 7. In the remaining 3 patients treatment had to be stopped on the 5th, 6th, and 7th days respectively because of deterioration in the clinical condition. These results are considered to be comparable with those obtained with emetine gr. 1 (65 mg.) daily for 10 days, but inferior to those obtained with aureomycin 2 g. daily for 15 days. The only toxic effect was a mild facial dermatitis which developed in 14 of the patients receiving the larger dosage of fumagillin and subsided when administration of the drug ceased. *J. L. Markson*

1596. **Low Gametocyte Thresholds of Infection of *Anopheles* with *Plasmodium falciparum*. A Significant Factor in Malaria Epidemiology**

R. C. MUIRHEAD-THOMSON. *British Medical Journal* [*Brit. med. J.*] **1**, 68–70, Jan. 9, 1954. 12 refs.

The infectivity of patients with malaria due to *Plasmodium falciparum* to mosquitoes has long been assumed to depend mainly on the number of gametocytes (crescents) in the blood, but it has recently been demonstrated that it is possible to infect mosquitoes experimentally from patients whose blood contains too few parasites to be detected on routine examination. In investigations carried out in the Accra district of the Gold Coast 73 batches of *Anopheles gambiae* were fed on 32 crescent carriers in a hyperendemic area; 24 of the batches fed on 14 of the carriers became infected. Of these 24 batches, 11 were infected from carriers in whom the crescent density was below 3 per 1,000 leucocytes, and in extreme cases less than 1 crescent per c.mm., densities which would probably not be recognized on ordinary routine thick-film examination. At these low densities 10% of the mosquitoes became infected, 1 or 2 oocysts being found per stomach in those infected, whereas with

the most highly infective carriers 30 to 40% of mosquitoes were infected, with an average of about 5 oocysts per stomach. Conversely, it was observed that several carriers with abundant crescents in the blood were non-infective to mosquitoes.

Infectivity thus does not appear to be directly related to crescent density, and low-density carriers (cryptic infectors), who are typically adults and older children, are probably of greater epidemiological importance than has been thought. This is supported by the finding that anophelines tend to bite adults and older children more frequently than young children and infants and that, in the present experiments, the highest proportion of non-infective carriers was found in the group aged 0 to 1 year. Similar findings have been reported from Jamaica and from South Carolina. *R. Crawford*

1597. **Field Studies of Some of the Basic Factors Concerned in the Transmission of Malaria**
G. DAVIDSON and C. C. DRAPER. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **47**, 522–535, Nov., 1953. 2 figs., 19 refs.

The relationships between the various factors involved in the transmission of malaria have been studied in the valley of the Sigi river in the Eastern Usambara mountains of Tanganyika, where infection with *Plasmodium falciparum* is almost universal (" holo-endemic "). The factors investigated included the splenic and parasite indices for the local population, the egg-laying habits, house-haunting propensities, biting cycles, and food preferences of the female anopheline vectors, and their survival rates, sporozoite rates, and infectivity rates.

The inoculation rate in infants, as shown by analysis of the parasite indices, was found to be 10 to 100 times less than the theoretical rate as calculated from entomological data, and it is suggested that this discrepancy is chiefly due to suppression by the infant of the majority of sporozoite infections before parasitaemia can occur. This suppression of infection is present from birth and may be due to the inhibiting effect of a milk diet.

[Many interesting points about transmission and control are brought out in this stimulating paper.]
*Clement Chesterman*

1598. **MSb and MSbB in the Treatment of Sleeping Sickness Due to Infection with *Trypanosoma gambiense***
E. A. H. FRIEDHEIM. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **47**, 350–360, Dec., 1953. 15 refs.

The author quotes the figures reported by himself and other workers for acute toxicity in mice and chronic toxicity in rats of both polymerized *p*-melaminylphenylstibonic acid (MSb) and 4-melaminyl-1-[methylol*cyclo*-(ethylenedithiastibina)] benzene (MSbB). The single-dose acute toxicity tests on both compounds showed the $LD_{50}$ to $CD_{50}$ ratio to be of the order of 100, the trivalent compound being considerably more toxic and proportionately more active than the pentavalent compound. Chronic toxicity tests showed the upper limit for 30 daily doses to be in the region of 50 mg. per kg. body weight for MSb and 2·5 mg. per kg. for MSbB. [Rollo *et al.* are wrongly quoted as having tested MSbB; the compound tested by the abstracter and colleagues was in fact the di-sodium di-thioglycollate of *p*-melaminylphenylstibonoxide, which appears to be slightly more toxic and slightly less active than MSbB.]

In clinical trials in French Guinea on 149 patients with trypanosomiasis due to *Trypanosoma gambiense* the pentavalent MSb was found to have a relatively slow but long-lasting trypanocidal effect, whereas the trivalent MSbB killed trypanosomes rapidly in lymph-node juice, blood, and in the central nervous system, but sustained administration, for at least 10 days, was necessary to ensure a permanent cure. Combined treatment with MSb given intramuscularly and MSbB orally gave good results and enabled the duration of treatment to be shortened. In first-stage cases 5 doses of MSb (10 mg. per kg. body weight, with a maximum dosage of 500 mg.) and 4 doses of MSbB, each of 5 to 8 mg. per kg. [an arithmetical error in the text gives the range as 5 to 80 mg. per kg.], given over a period of 7 days resulted in cure in 90% of cases observed in a 21-month follow-up. In second-stage cases 5 doses of MSb and 4 doses of MSbB over 7 days gave a high proportion of cures, while in cases treated with a greater number of doses no relapses were observed during a follow-up period of 15 to 28 months.

The author points out that the number of cases is too small for statistical evaluation, and suggests that the optimum combination of the two drugs is yet to be arrived at. The combined treatment was well tolerated and side-effects were negligible. There was no evidence of encephalopathy or of peripheral neuritis, even with doses above the therapeutic level, in contrast to the findings in cases treated with the analogous melaminyl arsenicals. *I. M. Rollo*

1599. **Histoplasmin Sensitivity and Pulmonary Calcification in Kenya**
H. STOTT. *British Medical Journal* [*Brit. med. J.*] **1**, 22–25, Jan. 2, 1954. 8 refs.

Calcification was observed in the chest radiographs of Suk tribesmen in Kenya who gave a negative Mantoux reaction to 1 mg. of old tuberculin. This suggested that the pulmonary calcification might be due to a mycotic infection, and the author therefore tested the histoplasmin sensitivity of a number of adult African males. Of 768 males tested, 65 (8·5%) gave a positive reaction to 1:100 histoplasmin, a positive reaction being defined as an area of induration of 5 mm. or more after 72 hours. Of 130 chest radiographs examined, 16 (12·3%) showed calcification, and of these 16 subjects, 8 reacted to both tuberculin and histoplasmin, 6 to tuberculin alone, and 2 to histoplasmin alone. In 10 cases there was a single area of calcification in the lung fields; in 5 cases there was calcification at the hilum as well as in the lung; and in one case evidence of calcification was seen at the hilum only. The author states that a diagnosis of histoplasmosis should be considered when persistent pulmonary infiltration is associated with a negative reaction to the tuberculin test. *Arthur Willcox*

# Allergy

1600. **Influence of Cortisone on Induced Asthma and Bronchial Hyposensitization**

H. HERXHEIMER. *British Medical Journal* [*Brit. med. J.*] **1**, 184–187, Jan. 23, 1954. 9 refs.

An investigation was carried out at University College Hospital, London, to determine whether cortisone would influence an induced asthmatic attack. Asthma was induced by allowing the patient to inhale the appropriate allergen, and the intensity of the attack was judged by the time taken to induce it and the reduction in the vital capacity. Of 11 patients tested, 5 reacted "immediately"—that is, 2 to 10 minutes after exposure; the remaining 6 were "late reactors"—that is, the asthmatic attack occurred 7 to 16 hours after exposure. The patients were given cortisone, and when under its influence were exposed to double or treble the amount of allergen which had previously caused a mild attack of asthma. This exposure was repeated after the dose of cortisone was reduced and after administration of the drug ceased. It was found that after all three exposures to the allergen, the asthmatic attack in the immediate reactors was mild and transient; in the late reactors no asthmatic attack was produced. It is concluded that cortisone abolishes or modifies the violence of the reaction to an overdose of allergen, and prevents hypersensitization while permitting the development of hyposenitization. *A. W. Frankland*

1601. **Experiences with Tetraethyl Ammonium Chloride in Bronchial Asthma**

L. GREGORY, M. DAMIANI, M. JOHANSON, A. ORMSBY, and A. RUSKIN. *Diseases of the Chest* [*Dis. Chest*] **24**, 655–662, Dec., 1953. 5 figs., 13 refs.

The effect of tetraethylammonium chloride (TEAC) on respiratory function during spontaneous or histamine-induced attacks of bronchial asthma was investigated in 20 subjects at the University of Texas Medical Branch, Galveston, and compared with those of adrenaline and aminophylline. After the intravenous administration of TEAC in a dose of 7 mg. per kg. body weight a rise in vital capacity of at least 25% was observed on 16 occasions, but there was no change on 13 others, and on 6 there was a reduction of over 25%, accompanied by increased dyspnoea and apprehension. Dyspnoea and bronchospasm were relieved—often within one or two minutes—in cases responding to TEAC, and mild attacks generally subsided rapidly. TEAC was effective in 2 out of 5 cases resistant to adrenaline, but in neither of 2 cases resistant to aminophylline.

In contrast, a significant reduction in vital capacity never occurred after the intramuscular injection of 0·2 to 0·6 mg. of adrenaline or after the intravenous injection of 0·24 to 0·48 mg. of aminophylline, a rise of 25% or more occurring with both drugs in most cases. Studies of the eosinophil count, urinary uric acid:creatinine ratio, and serum electrolyte levels failed to provide evidence that TEAC stimulated the adrenal cortex to any significant degree. One patient died after receiving 0·2 g. of TEAC intravenously, having developed severe hypotension unrelieved by adrenaline.

The effect of TEAC on asthma is considered to be due primarily to the relief of vagotonic bronchospasm resulting from ganglion blockade, but it may also be due in part to a decrease in pulmonary arterial pressure and an increase in sensitivity to adrenaline. Each individual's response to the drug is unpredictable, however, and its use is not free from risk, particularly in the presence of heart disease, owing to the systemic hypotension which it induces. *K. Gurling*

1602. **Fatal Bronchial Asthma. A Review of 18 Cases**

C. K. ROBERTSON and K. SINCLAIR. *British Medical Journal* [*Brit. med. J.*] **1**, 187–190, Jan. 23, 1954. 18 refs.

The clinical and post-mortem findings in 18 fatal cases of asthma are analysed in this paper from the Royal Infirmary, Edinburgh. Most of the patients were between 40 and 50 years of age, 11 being females and 7 males. The duration of the disease in this series was unrelated to the fatal outcome. In 13 cases death was sudden and unexpected and in 5 it followed progressive exhaustion and coma. Although three aetiological factors were recognized—psychological, allergic, and infective—it was found that more than one of these could be operative in the same patient at the same time. Occlusion of the bronchi by plugs of tenacious mucus was seen macroscopically and microscopically in all cases. *A. W. Frankland*

1603. **Studies on Factors Influencing Ragweed Pollen Counts in the New York Metropolitan District. I. Pollen Studies on Ambrose Lightship in New York Harbour**

R. D. WISEMAN, S. S. SACK, B. B. SIEGEL, I. GLAZER, and M. WALZER. *Journal of Allergy* [*J. Allergy*] **25**, 1–11, Jan., 1954. 5 figs., 11 refs.

For many years allergologists of the Jewish Hospital, Brooklyn, have made daily ragweed-pollen counts by exposing greased slides at various points in the New York area. In this paper the authors report those made on the Ambrose lightship, which is moored to the south of New York harbour, 9 miles (14·5 km.) from the land. When westerly winds prevailed, the pollen counts on the lightship were between 40% and 60% of the counts obtained in New York City. It is concluded that New York receives almost as much wind-borne ragweed pollen from outside as it produces within its own city borders. [If this is correct, it will hold also for other big towns.] *H. Herxheimer*

# Nutrition and Metabolism

1604. **On the Nutritional Requirements of Young Children with Particular Reference to Calcification**
T. ALLEN, A. V. MACLEOD, and E. G. YOUNG. *Canadian Journal of Medical Sciences* [*Canad. J. med. Sci.*] **31**, 447–461, Dec., 1953. 1 fig., 39 refs.

The authors report the results of two dietary and nutritional surveys of groups of pre-school children in Halifax, Nova Scotia: (1) carried out on 55 children of the wealthier classes in 1945–47; and (2) carried out on 103 of the poorest class in 1949–51. Food consumption was determined by individual weighing, and physical examination repeated after 6 months. The purpose was to correlate the dietary data with physical findings and rate of growth, to determine the requirements of children of this age for some of the essential nutrients, and to compare these values with those which are commonly accepted, but have little factual basis.

According to dietary standards drawn up by the Canadian Council on Nutrition the intake, especially of children of Group 2, was commonly deficient in calories, calcium, and vitamin D; for example, 47% of the children in Group 1 and 84% of those in Group 2 received less than the recommended daily minimum of 400 I.U. of vitamin D, while 78% of all the children received less than the standard of 1 g. of calcium daily. Nevertheless, growth and calcification were not necessarily retarded and in some cases an intake of 200 to 700 mg. of calcium and 25 to 150 I.U. of vitamin D was clearly adequate.

[The correlative study of dietary intake and physical state is an important method of assessing the nutrient requirements of human subjects; it is, however, not at all easy to determine the former accurately. In this study each child's intake was measured for one week, and few details of the method are given; but it is known that even when all precautions are taken, such a period is not sufficient for accurate assessment. The results would also have been more useful if details had been given of the physical findings in relation to intake in individual cases.] *John Yudkin*

1605. **Liver Function during Intravenous Infusion of Emulsified Fat to Humans**
W. R. WADDELL, T. B. VAN ITALLIE, R. P. GEYER, and F. J. STARE. *Annals of Surgery* [*Ann. Surg.*] **138**, 734–740, Nov., 1953. 15 refs.

The effect on liver function of intravenous administration of a fat emulsion was investigated in 21 malnourished patients in a surgical ward at the Massachusetts General Hospital, Boston. Liver biopsy and a battery of liver function tests were carried out, and in some cases necropsy specimens were examined, though death was not due to the fat infusion. The emulsion consisted of 15% coconut or olive oil homogenized with 1% soya-bean phosphatide and 1% polyglycerol ester of oleic acid; it was stable during storage and in blood. The liver function tests included the "bromsulfalein" retention and cephalin flocculation tests, estimation of the serum level of bilirubin, alkaline phosphatase, cholesterol and cholesterol esters, and albumin and globulin, and determination of the plasma prothrombin time. No consistent alterations in liver function were noted, though there was some impairment in patients undergoing operation during the observation period, this being considered in accordance with the changes to be expected after anaesthesia and operation.

The authors conclude that repeated intravenous administration of emulsified fat has no deleterious effect on liver function. *J. M. French*

1606. **The Influence of Caloric and Potassium Intake on Nitrogen Retention in Man**
J. M. BEAL, P. M. FROST, and J. L. SMITH. *Annals of Surgery* [*Ann. Surg.*] **138**, 842–845, Dec., 1953. 3 figs., 7 refs.

It is generally agreed that an adequate caloric intake is necessary to prevent excessive loss of nitrogen, and Cannon *et al.* have recently shown (*Metabolism*, 1952, **1**, 49) that the presence of certain electrolytes, notably potassium, are also necessary for satisfactory protein metabolism. In the study here reported from the Veterans Administration Center Hospital, Los Angeles, of 3 surgical patients who were receiving nutrition parenterally, it was found that a positive nitrogen balance was achieved and maintained by administration of a solution supplying 500 g. of glucose in the form of 25% solution in 5% alcohol, 16 g. of nitrogen as protein hydrolysate, and 80 mEq. of potassium per day. Omission of the potassium resulted in a return to negative nitrogen balance. *F. W. Chattaway*

1607. **Survival of Transfused Red Cells in Scurvy**
C. MERSKEY. *British Medical Journal* [*Brit. med. J.*] **2**, 1353–1356, Dec. 19, 1953. 2 figs., 11 refs.

The survival of transfused erythrocytes was studied at the Groote Schuur Hospital, Capetown, in 9 patients (8 Bantu and one Indian) with typical scurvy, 8 of whom were anaemic. On admission they were given a diet entirely lacking ascorbic acid and after a short control period a transfusion of 2 to 4 pints (1·1 to 2·3 litres) of citrated stored blood was given in each case. The survival time of the transfused cells, as determined by the Ashby technique, was abnormally short in 6 cases; this was apparently due to haemolysis, as there was no evidence of haemorrhage. But an odd finding was that the fall in the haemoglobin level after the transfusion seemed in 4 cases to be more rapid than that usually observed when patients with scurvy are simply kept in

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bed on a deficient diet without transfusion. Moreoever, in some cases the abnormal rate of erythrocyte destruction persisted for some days after treatment with ascorbic acid was begun. The author considers, however, that there is adequate evidence that haemolysis is an important factor in the pathogenesis of the anaemia of scurvy.

(In an addendum brief details are given of similar studies on a further 9 scorbutic patients, in 8 of whom erythrocyte survival was much shortened. In 5 of these cases a replacement transfusion was given, so that the haemolysis could not be attributed to over-transfusion.)

*M. C. G. Israëls*

1608. **Relationship of Body Composition to Basal Metabolic Rate in Normal Man**

R. J. WEDGWOOD, D. E. BASS, J. A. KLIMAS, C. R. KLEEMAN, and M. QUINN. *Journal of Applied Physiology* [*J. appl. Physiol.*] **6**, 317–334, Dec., 1953. 5 figs., bibliography.

In this paper the authors suggest that the usual practice of relating the basal metabolic rate (B.M.R.) to the body surface area is not entirely satisfactory. They have therefore studied the B.M.R. of 17 normal male subjects, ranging in age from 19 to 29 years, in relation to their height, weight, surface area, plasma volume, extracellular and intracellular fluid volume, total body water, and interstitial fluid volume, all of which were determined or calculated by standard methods.

Analysis of the results by the method of partial correlations indicated that the relationship between the B.M.R. and surface area is not a primary one, but depends on an underlying relationship of each of these variables to the extracellular or to the interstitial fluid volume; changes in interstitial fluid volume accounted for 41% of the total variability observed in the B.M.R., and for as much as 63% of that part of the observed variability which could be predicted from the various measurements taken. Changes in intracellular fluid accounted for a further 28% of the predictable variation, but the volume of intracellular fluid was negatively correlated with the B.M.R. These results are interpreted by the authors as supporting the view of Robinson (*Proc. roy. Soc. B.*, 1950, **137**, 378) that increase in cell metabolism favours water transport from intracellular to extracellular fluid.

[Although this paper suggests that body water would be a more accurate reference than surface area for standardizing B.M.R. estimations on different subjects, there is enough relationship between body water and surface area to justify retaining the latter as a practical reference for all ordinary purposes.]

*D. A. K. Black*

1609. **Potassium and Tetany.** (Kalium und Tetanie)

G. FANCONI and T. NEUHAUS. *Helvetica paediatrica acta* [*Helv. paediat. Acta*] **8**, 424–450, Nov., 1953. 6 figs., 38 refs.

After a review of the literature concerning the influence of potassium on nervous excitability, the authors report observations made in a series of cases at the University Paediatric Clinic, Zürich, which seem to confirm the existence of such an influence. These cases fell into four groups: (1) In 4 children, one aged 7 months and the others between 14 and 16 years, with acute nephritis, "uraemic" convulsions occurred only when hyperpotassaemia was present, and their relief was related more closely to the restoration of a normal blood potassium level than to reduction of the blood non-protein nitrogen level or the blood pressure. (2) In 3 cases of neonatal tetany (one of them fatal) hypocalcaemia (due to transient or persistent hypoparathyroidism) was associated with hyperpotassaemia and a high K:Ca ratio. (3) Convulsions occurred in 2 infants, aged 4 and 3½ months respectively, suffering from toxic dehydration; in the first case these followed the administration of an intravenous drip infusion of a solution containing potassium which caused a rise in blood potassium level to 40 mg. per 100 ml., and in the second hypocalcaemia and hyperphosphataemia were combined with hyperpotassaemia. (4) In 4 children aged 12 to 14½ years, all of whom were "highly strung" and showed signs of abnormal lability of the autonomic nervous system, the characteristic signs of latent tetany were present although the blood calcium level was normal. The blood potassium level, however, was increased in every case, and ranged from 20·2 mg. per 100 ml. to 23·3 mg. per 100 ml. (normal 16 to 20 mg. per 100 ml.), repeated estimations being made in 2 of the 4.

*V. C. Medvei*

1610. **Cation Uptake by Exchange Resin *in vitro* and the Colon as a Sodium-conserving Organ**

H. FIELD, L. SWELL, D. F. FLICK, and R. E. DAILEY. *Circulation* [*Circulation* (*N.Y.*)] **9**, 32–37, Jan., 1954. 24 refs.

1611. **Porphyria**

G. DEAN. *British Medical Journal* [*Brit. med. J.*] **2**, 1291–1294, Dec. 12, 1953. 15 refs.

Porphyria is a serious familial disorder involving the pyrrole pigments which take part in respiratory metabolism, and is fairly common in South Africa. In this paper from the Provincial Hospital, Port Elizabeth, 12 cases of porphyria occurring in 11 Afrikaner families are described.

In the chronic stage of the disease symptoms of neurotic origin, particularly abdominal pains, are often the main complaint, and the importance of recognizing this is emphasized; porphyrins may be absent from the urine at this stage, and a full personal and family history may be required in order to make diagnosis certain. An acute attack may occur during pregnancy or following an abdominal operation, and may be precipitated by the use of various sedatives, particularly barbiturates. The use of barbiturate anaesthetics, especially thiopentone, may result in paralysis. In acute attacks, porphyrins are always present in the urine. The diagnosis, differential diagnosis, and treatment are discussed, and 7 brief illustrative case histories are given. It is urged that when a case is discovered, as many near relations of the patient as possible should be examined, as thereby much unnecessary suffering may be prevented.

*F. W. Chattaway*

# Gastroenterology

1612. **Studies on Pancreatitis**
E. G. SAINT and S. WEIDEN. *British Medical Journal* [*Brit. med. J.*] **2**, 1335–1340, Dec. 19, 1953. 10 figs., bibliography.

The clinical features, aetiology, diagnosis, and treatment of acute and chronic pancreatitis were studied at the Walter and Eliza Hall Institute of Medical Research and the Royal Melbourne Hospital, 11 cases of acute and 13 cases of chronic pancreatitis of varied origin being investigated. The tests performed included the estimation of urinary diastase, intravenous secretin test, histamine test meal, a number of liver function tests, liver biopsy, and oral glucose tolerance test. In 4 cases the tryptic activity of the pancreatic juice was estimated by means of a gelatin absorption test. Radiographs of the pancreatic area, barium-meal examinations, and cholecystograms were also carried out.

Although the estimation of urinary diastase was found to be of great help if carried out within 2 to 5 days of the onset of acute pancreatitis, attention is drawn to the inadequacy of laboratory tests generally as aids to diagnosis in both conditions, the intravenous secretin test being particularly disappointing. Difficulty was encountered in a number of cases in making a definite diagnosis without recourse to exploratory laparotomy, and it is suggested that aspiration biopsy of the pancreas should be carried out in addition to inspection and palpation when such an operation is undertaken.

The need for electrolyte replacement and antibiotics in the treatment of acute pancreatitis is stressed, and the different types of procedure for relief of pain in chronic pancreatitis are discussed. *J. M. French*

1613. **The Bacterial Content of Human Small Intestine in Disease of the Stomach**
J. CREGAN, E. E. DUNLOP, and N. J. HAYWARD. *British Medical Journal* [*Brit. med. J.*] **2**, 1248–1251, Dec. 5, 1953. 11 refs.

In a previous paper (*Brit. med. J.*, 1953, **1**, 1356) two of the authors showed that in healthy persons the small intestine is not colonized by a resident bacterial flora, the few bacteria found being transient contaminants passing through with the ingesta. In the present paper from the Royal Melbourne Hospital (University of Melbourne) an investigation of the bacterial flora of patients with disease of the stomach is reported. At operation the contents of the intestine were aspirated with a syringe and examined bacteriologically, samples being taken from the upper jejunum and middle and lower ileum. It was found that even when the gastric acidity was low and the stomach was heavily contaminated there were few, if any, bacteria in the middle ileum. It is suggested that the small intestine possesses an antibacterial mechanism which is independent of the gastric germicidal barrier; furthermore, that there is no foundation for the common belief that after gastrectomy or in cases in which the gastric secretions are otherwise reduced the organisms of the colon invade the small intestine.
*D. G. ff. Edward*

## PHARYNX AND OESOPHAGUS

1614. **Motor Mechanisms of the Esophagus, Particularly of its Distal Portion**
G. C. SANCHEZ, P. KRAMER, and F. J. INGELFINGER. *Gastroenterology* [*Gastroenterology*] **25**, 321–332, Nov., 1953. 8 figs., 14 refs.

The authors report the results of an investigation into the swallowing mechanism carried out at Boston University School of Medicine by means of fluoroscopy and the recording of intra-oesophageal pressure. Two No. 10 intravenous catheters, attached to each other so that their distal ends were 8 cm. apart, were passed into the oesophagus, filled with water, and pressures recorded with an electromanometer as in the measurement of intra-arterial pressure.

Recordings taken from the upper seven-eighths of the oesophagus during swallowing showed first a small positive wave due to filling of the organ with fluid; this was followed in about 5 seconds by a pressure of 40 to 110 mm. Hg lasting approximately another 5 seconds which was shown to be due to a peristaltic wave travelling at the rate of 2 cm. per second. This wave did not depend on the presence of swallowed material, as it also occurred after a "dry" swallow. In one subject, a patient with bulbar paralysis, no initial pressure wave was found, as no material entered the oesophagus, but the peristaltic wave appeared nevertheless. Though initiated by swallowing, this peristalsis was also inhibited by it, so that when repeated attempts were made to swallow, it did not occur until the last attempt had taken place. Gravity had no effect on this reflex mechanism.

The distal 2 to 5 cm. of the oesophagus is divided into two parts, the ampulla and vestibule. The ampulla was found to be functionally a part of the upper portion of the oesophagus and was subject to the positive pressure which developed immediately on swallowing. The second, peristaltic, wave did not rapidly fall away as in the upper oesophagus, but lasted from 15 to 20 seconds. This did not appear to be due to the failure of the cardia to relax but rather to slowing of the peristaltic wave and maintenance of muscle contraction. Normal responses were obtained in subjects with hiatus hernia and paralysis of the left diaphragm.

The vestibule or terminal 2 or 3 cm. of the oesophagus appeared to be functionally independent of the remainder of the organ, the absence of the first positive pressure suggesting that it was not in contact with the remainder of the lumen. Also, pressure changes in it were gradual, never rising above 15 mm. Hg, and the peristaltic wave

was not propagated into the vestibule. The authors suggest that vestibular function may be at fault in such conditions as hiatus hernia and achalasia, and point out that an abnormally functioning vestibule may clinically and radiographically mimic a small sliding hernia and result in reflux oesophagitis.

[Neither the number of subjects tested nor the number of experiments made is given.] *A. G. Parks*

1615. **The Disturbance of Esophageal Motility in Cardiospasm: Studies on Autonomic Stimulation and Autonomic Blockade of the Human Esophagus, Including the Cardia**
M. H. SLEISENGER, H. STEINBERG, and T. P. ALMY. *Gastroenterology* [*Gastroenterology*] **25**, 333–348, Nov., 1953. 11 figs., 29 refs.

By the use of intra-oesophageal balloons to measure the pressure and of fluoroscopy to visualize the activity of the lower oesophagus, the authors have attempted to determine the fundamental lesion causing achalasia. The experiments were carried out at the New York Hospital–Cornell Medical Center, New York, on 21 patients with cardiospasm, 13 normal individuals, and 6 patients with varied oesophageal conditions, including malignancy.

The effect of methacholine chloride on the normal oesophagus was found to be negligible. In patients with achalasia, however, it produced increased tone and decreased phasic activity, and fluoroscopy in these cases showed increased contraction of the oesophagus but no relaxation of the cardiac sphincter. The drug had a similar effect on patients in whom cardiac delay had been relieved by operation. It had no action on patients with conditions other than achalasia. Acetylcholine had a similar though less constant effect. Neostigmine caused no alteration in oesophageal behaviour in either patients or normal subjects. In these experiments enough of each drug was administered to produce flushing and sweating.

"Banthine" (methantheline) was the only anticholinergic drug investigated; it was found to inhibit both spontaneous and methacholine-induced visceral tone, but it had no effect on delay at the cardiac orifice. The sympathicomimetic drugs, adrenaline and noradrenaline, produced no reaction in normal subjects, but inconstantly reduced the tone in some cases of achalasia. The adrenergic blocking drugs, "dibenzyline" and "regitine", administered in sufficient quantity to produce orthostatic hypotension, failed to have any action on oesophageal activity. Tetraethylammonium chloride likewise was without effect.

The exaggerated response of the oesophageal musculature to methacholine in patients with achalasia, combined with the absence of response to neostigmine, suggested that it was not receiving a normal amount of cholinergic innervation. That these effects are not due to obstruction *per se* is evident from the fact that they persist after operative relief of obstruction, and do not occur with other obstructing lesions. These findings therefore give no support to the view that sympathetic overactivity plays a part in producing achalasia. The evidence obtained points to an incoordination (and perhaps a deficiency in the quantity) of parasympathetic innervation as being the likely cause of this condition.

*A. G. Parks*

1616. **The Surgical Management of Achalasia of the Esophagus**
H. R. HAWTHORNE and P. NEMIR. *Gastroenterology* [*Gastroenterology*] **25**, 349–358, Nov., 1953. 3 figs., 6 refs.

At the University of Pennsylvania Hospital, Philadelphia, 22 patients with achalasia of the cardia were studied before and after the performance of oesophago-cardio-myotomy (Heller's operation). Preoperatively, oesophagoscopy had revealed the usual dilatation, but the mucosa was invariably found to be normal and without any signs of inflammation. The operation was performed through the abdomen; after division of the left triangular ligament of the liver, traction was applied to the lower oesophagus and a longitudinal incision made down to the mucosa in the last 2½ inches (6 cm.) of the oesophagus and the adjacent 1½ inches (4 cm.) of the cardia. One patient died from cerebral haemorrhage 5 days after operation. In 3 other patients the results were unsatisfactory owing to complications; in the first, operation revealed a carcinoma of the oesophago-gastric junction, another had recurrent severe oesophagitis with haematemesis, and gastrectomy had later to be performed, while the third had severe symptoms of gastric reflux.

However, the results of operation in the remaining 18 cases were excellent; in all of them the dysphagia was completely relieved and the patients were able to return to a normal diet, although 4 of them had occasional symptoms of acid regurgitation and heartburn. In about half the patients gastric reflux could be induced by placing them in the Trendelenburg position and performing the Valsalva manœuvre. The authors point out that although the results of the operation are excellent as a rule, the cardiac obstruction is frequently replaced by incompetence, which may result in oesophagitis as a late complication. *A. G. Parks*

1617. **Achalasia of the Cricopharyngeal Sphincter**
N. ASHERSON. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **20**, 531–543, Nov., 1953. 9 figs., 22 refs.

The author has made it a routine practice to take lateral radiographs made in conjunction with a barium swallow—pharyngograms—in all cases of laryngeal disease seen by him over the last 15 years, including those due to neurological disorders. From among those of the latter group has emerged a characteristic radiological picture, in which a failure of the cricopharyngeus muscle to relax at the proper time is seen. This achalasia, occurring at the entrance to the oesophagus, corresponds to cardiospasm at the exit, and "in the past has invariably masqueraded under the soubriquet of 'vallecular dysphagia'".

In this paper the author proffers a new interpretation of this recognized lesion. Normally, two extremely rapid reflex mechanisms precede the passage of a swallowed bolus, namely, closure of the glottis and relaxation

of the cricopharyngeus muscle. This action depends, of course, on an intact neuromuscular arc involving the spinal accessory, vagus, and recurrent laryngeal nerves. A break anywhere in the chain, such as operative division of the musculature by pharyngectomy or a lesion of the recurrent laryngeal nerve, results in incoordination. In cricopharyngeal achalasia relaxation is delayed and is also incomplete, but there is no mechanical obstruction. In the pharyngogram the hypopharynx appears elongated, the bolus is seen to be arrested above the cricopharyngeus, there is retention or overflow, and great delay in emptying the pharynx. The commonest causes are anterior poliomyelitis and recurrent paralysis; the condition is much more severe in bilateral palsies.

Clinically, symptoms may be entirely absent in some cases, and the diagnosis is then essentially radiological. Other patients notice mild dysphagia, especially for liquids, or a persistent feeling of " something in the throat ". Mirror examination shows an accumulation of saliva which may overflow into the larynx, producing a cough. In diagnosis the condition must be differentiated from postcricoid cancer, pharyngeal pouch, impacted foreign body, and sideropenic dysphagia. Illustrative histories of 10 cases are briefly described.

*M. Meredith Brown*

## STOMACH

1618. **Mallory–Weiss Syndrome. Hemorrhage from Gastroesophageal Lacerations at the Cardiac Orifice of the Stomach**

J. P. DECKER, N. ZAMCHECK, and G. K. MALLORY. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 957–963, Dec. 10, 1953. 4 figs., 29 refs.

Haematemesis from lacerations of the oesophagus and cardia caused by protracted vomiting or retching (the Mallory–Weiss syndrome) has been almost completely neglected in the literature since its first description in 1932. Typically the lacerations range from 0·5 to 3·0 cm. in length and up to 0·7 cm. in width and usually involve both oesophagus and stomach, the cardio-oesophageal junction passing through the middle. Microscopically the lesions appear as flattened or trench-shaped ulcers based on the submucosa or muscularis mucosae, the walls containing extravasated blood cells, while in older lesions there is granulation tissue.

The authors describe 5 cases in detail and summarize 6 others, all of which occurred during a 20-year period among a total of approximately 11,000 necropsies performed at Boston City Hospital (Harvard Medical School). These cases fall into three groups: (A) Five cases (2 in patients over the age of 80) in which the laceration was thought to be the main cause of death. [The cases of the youngest 2 patients in this group, aged 50 and 52 respectively, are not described in detail.] (B) Four cases with grave associated disease—a perforated ulcer with peritonitis, cerebral thrombosis, uraemia from polycystic disease, and calculous pancreatitis. (C) Two cases in which there was alcoholic or nutritional cirrhosis. Severe vomiting preceded the bleeding in all cases and is assumed to have caused the lacerations. Atrophic gastritis was present in 6 out of 8 cases in which the mucosa was examined microscopically, and was possibly a contributory factor.

[This condition should be compared with that described as " spontaneous rupture of the oesophagus ".]

*Denys Jennings*

1619. **Analysis of 1,000 Gastroscopically Examined Cases.** [In English]

M. SIURALA and M. LEHTINEN. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **42**, 293–305, 1953. 2 figs., 22 refs.

In this paper from the University of Helsinki the authors analyse the gastroscopic findings in a series of 1,000 cases, pointing out that although many similar analyses have been published (this is the first to appear in the Finnish literature), in relatively few of them are the findings correlated with the results of histological examination of biopsy specimens of the gastric mucosa. In their series specimens were obtained with a suction tube, a modified version of Wood's biopsy punch, from 332 patients, but in 32 cases difficulty was encountered in interpreting the findings. The histological picture " differed somewhat " from the gastroscopic appearances in 62 cases, but confirmed the diagnosis in 238 cases. In only 16 cases was it " completely different " from the gastroscopic picture [the authors do not discuss these 16 interesting cases].

The series included 87 cases of gastric ulcer, 88 of duodenal ulcer, 10 of pyloric ulcer, 46 of gastric carcinoma, 13 of benign tumour, 14 of gastric resection, and 50 of megaloblastic anaemia. Of the remaining 692 cases superficial, hypertrophic, or atrophic gastritis was found in 305 and a normal stomach in 387. The authors' main findings were that: (1) gastroscopy was slightly more reliable than radiology in the diagnosis of gastric ulcer and gastric carcinoma; (2) the incidence of atrophic gastritis increased with age; (3) a normal gastric mucosa was present in 35 of the 87 cases of gastric ulcer and in 37 of the 88 cases of duodenal ulcer. Hypertrophic gastritis was the dominating type of change in duodenal ulcer, and atrophic or superficial gastritis in gastric ulcer.

*I. McLean-Baird*

1620. **Peptic Ulcer: Late Follow-up Results after Partial Gastrectomy: Analysis of Failures**

H. D. HARVEY, F. B. ST. JOHN, and H. VOLK. *Annals of Surgery* [*Ann. Surg.*] **138**, 680–688, Nov., 1953. 20 refs.

In 1948 the authors reported the follow-up results of partial gastrectomy for peptic ulcer in a series of 394 patients operated on in the years 1936 to 1945 (*Ann. Surg.*, **128**, 3). In the present paper further progress is reported, together with results obtained at the Presbyterian Hospital (Columbia University), New York, in a second series of 504 patients operated on between 1946 and 1950. In the first series a Polya type of resection was performed, and in the second a more radical gastrectomy with a Hofmeister anastomosis. Of the total of 898 patients, 232 had gastric ulcer and 666 duodenal ulcer.

Of the 298 patients with duodenal ulcer in the first series, 257 were considered to be " wholly satisfactory "

in 1946 and 248 were still " wholly satisfactory " 5 years later. Corresponding figures for 96 patients with gastric ulcer were 82 in 1946 and 75 in 1951. The operative mortality fell from 4·6% before 1946 to 1% in the 5 years after 1946. Ulceration recurred in 4% of the patients in whom gastrectomy was performed for duodenal ulceration before 1946 and in 5·2% of the similar group in the second series. The recurrence rate in the patients with gastric ulcer was negligible.

In the second series, in which more extensive gastrectomy was carried out, severe degrees of the dumping syndrome were more common than in the first, and were present at some time in one-third of the patients; in about 13% these symptoms persisted. Considerable loss of weight was also commoner in patients undergoing radical gastrectomy. The authors state that they now favour a less extensive gastrectomy combined with abdominal vagotomy. *D. W. Barritt*

1621. **A Study of Acute Gastric Ulcers Causing Haemorrhage**

F. Avery Jones and W. E. King. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **2**, 179–185, Nov., 1953. 2 figs., 2 refs.

The authors discuss the prognosis in, and the immediate mortality from, acute gastric ulcer causing haemorrhage, and then compare the clinical features with those observed in cases of chronic gastric ulcer. Between 1941 and 1951 inclusive 1,223 patients were admitted to the Central Middlesex Hospital, London, for haematemesis or melaena from proved or probable peptic ulcer. In 377 of these, which were classified in the " acute ulcer " group, no cause for the haemorrhage could be found on radiological examination. Gastroscopy, which was performed between the third and tenth days after admission on 230 of the patients in this group, revealed acute gastric ulcer in 83. Analysis of the symptoms showed that the duration of pain was of little help in differentiating a case of acute from one of chronic ulcer, but the authors noted that when severe pain was recorded no acute ulcer was found.

It is pointed out that although the acute gastric ulcer may cause severe haemorrhage the mortality rate is low, except in patients over the age of 65 years. Further, surgical treatment must sometimes be considered, especially in cases of recurrent haemorrhage, although the site of the bleeding remains obscure. The prognosis is good in women, but chronic ulcers tend to occur subsequently in men. *I. McLean-Baird*

1622. **Acid Secretion in Various Conditions of the Gastric Mucosa. A Morphologic and Gastroscopic Study of 265 Histamine-examined Cases.** [In English]

M. Siurala and M. Lehtinen. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **42**, 306–313, 1953. 1 fig., 18 refs.

The authors at the University of Helsinki have attempted to correlate the gastroscopic and histological appearances with the acid-secreting power of the gastric mucosa in 265 selected cases, including 75 in which the stomach was normal, 136 cases of gastric mucosal atrophy, 14 of superficial gastritis, 10 of " atrophic-superficial " gastritis, 19 of hypertrophic gastritis, and 11 of mixed gastritis. A good correlation was observed between the gastroscopic and histological diagnoses.

It was found that after subcutaneous injection of 0·1 mg. of histamine phosphate per 10 kg. body weight the amount of hydrochloric acid secreted by the mucosa was inversely proportional to the severity and extent of the mucosal atrophy. However, free hydrochloric acid was detectable in 26% of the histologically and 23% of the gastroscopically diagnosed cases of " total " mucosal atrophy. The authors attribute this to the fact that neither gastroscopy nor mucosal biopsy indicate the condition of the whole of the stomach. Achlorhydria was found in 7 of the cases in which the mucosa appeared normal, this being due, it is suggested, to insufficient histamine stimulus. The ability of the stomach to secrete hydrochloric acid in superficial gastritis differed little from that of the normal stomach, but high free-acid values were observed in cases of hypertrophic gastritis. *I. McLean-Baird*

1623. **A Clinical Evaluation of a New Anticholinergic Drug, " Pro-Banthine "**

I. R. Schwartz, E. Lehman, R. Ostrove, and J. M. Seibel. *Gastroenterology* [*Gastroenterology*] **25**, 416–430, Nov., 1953. 2 figs., 12 refs.

" Pro-banthine " (propantheline) is the *iso*-propyl derivative of " banthine " (methantheline) and has a similar, but more potent, anticholinergic action, " without significant increase in toxicity ". The present report sets out the results of a year's experience of propantheline in the treatment of 156 patients with various gastrointestinal diseases at Kings County Hospital, Brooklyn, New York.

In 129 cases of peptic ulcer attention was directed especially to the relief of pain and rapidity of healing. The patients, 77 of whom had previously been treated with methantheline or with " prantal ", continued to take antacids, sedatives, and bland diet as prescribed before starting treatment with propantheline. The criteria of successful therapy included " amelioration of symptoms and lack of return of symptoms when recurrence would be expected "; by this standard, treatment was successful in 118 cases. Relief of pain in a severe case usually occurred within 48 to 72 hours of starting treatment with 30 to 45 mg. of propantheline every 6 hours, and after about 2 weeks at this dosage a maintenance dose of 15 mg. 6-hourly was adequate, while in mild or moderately severe cases the latter dose could often be given from the start. In 10 cases, however, symptoms recurred when the maintenance dosage was given, but were controlled by increasing the dose to 45 or 60 mg. every 6 hours for a few days in 7 of these. Of the other 3, in which only partial control was achieved, there was evidence of posterior penetration of a duodenal ulcer into the pancreas in 2, and a moderate degree of post-pyloric obstruction in the third. It is interesting that heartburn (relieved by antacid therapy) persisted in 14 cases after the characteristic pain had been relieved. Both clinically and radiologically, the rate of healing

was accelerated: 80 of the 116 duodenal ulcers had well-delineated craters, and 59 of these healed completely within 4 weeks and the other 21 within 8 weeks of starting treatment. In 10 cases of acute duodenal ulcer healing occurred in 2 to 4 weeks.

High doses of propantheline did not relieve the heartburn complained of by 2 patients with hyperacidity associated with chronic anxiety. In 6 cases of functional diarrhoea and 2 of diarrhoea following surgical treatment of regional ileitis 30 to 45 mg. of propantheline 4 times daily gave significant or complete relief, while some symptomatic benefit was claimed by 2 of 4 patients with chronic ulcerative colitis. One patient with the dumping syndrome also obtained complete relief while receiving propantheline.

All the patients who had previous experience of taking methantheline preferred propantheline as it caused fewer and less annoying side-effects. Of the 156 patients, 35 complained of dryness of the mouth, 17 of blurring of vision, 16 of headache, 19 of mild to moderate constipation, and 10 of difficulty of micturition. Urinary frequency occurred in 14 cases, with transient albuminuria, but after 2 or 3 weeks both frequency and albuminuria cleared up. Three patients complained of moderately severe palpitation, and 5 of transient drowsiness.

It is concluded that propantheline is an effective anticholinergic agent which diminishes the volume of gastric secretion and inhibits gastro-intestinal motility, with relatively slight side-effects which rarely require treatment to be stopped. *Derek R. Wood*

1624. **Vagotomy for Duodenal Ulcer. A Final Survey after Ten Years**
J. R. Brooks and F. D. Moore. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 1089–1097, Dec. 31, 1953. 24 refs.

The results of a follow-up investigation of 132 patients on whom vagotomy was performed for duodenal ulcer 6 to 10 years previously are reported in this paper from the Peter Bent Brigham Hospital (Harvard Medical School), Boston. In 82 of the patients vagotomy alone was carried out, in 36 vagotomy with gastro-enterostomy, and in 14 vagotomy after subtotal gastrectomy. The results did not compare favourably with those obtained in an earlier series of 175 cases in which gastrectomy was performed. Although about two-thirds of the 132 patients appeared to be symptom-free, the incidence of ulceration in the remainder was high.

It is pointed out that marginal ulceration may develop although the free-acid level is low and there is a delayed response to the insulin test. Conversely, there may be no symptoms and no radiological evidence of ulcer for 5 to 10 years despite a positive reaction to the insulin test and a high free-acid level. In the present investigation the authors found that with the passage of time there was an increase in the incidence of positive results to the insulin test and the free-acid levels became higher. The uropepsin level, however, remained within the abnormal range, being little affected by vagotomy.

In the authors' view vagotomy alone is not a satisfactory primary surgical procedure for duodenal ulcer, but it has a definite place in the treatment of marginal ulcer occurring after gastrectomy. Further, the results of vagotomy combined with gastro-enterostomy are disappointing; ulceration may recur while the physiological effects of vagotomy persist. *Guy Blackburn*

1625. **A Study on the Use of " Piromen " for the Treatment of Duodenal Ulcer in Man**
W. H. Olson and H. Necheles. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **20**, 372–380, Dec., 1953. 17 refs.

The authors have previously shown that gastric motility and gastric secretion are inhibited following injection of pyrogens without any rise in temperature. In this paper from the Michael Reese Hospital, Chicago, they describe an investigation of the action of " piromen ", a pyrogenic polysaccharide of bacterial origin, in 25 male inmates of a prison with active duodenal ulcer, 14 of the men being confined to bed for at least 4 weeks during treatment and 11 being ambulatory. The drug was given by subcutaneous injection in a dose of 10 mg. twice daily. No sedatives, antacids, or antispasmodics were given, and the patients received the usual prison diet with additional protein in the form of eggs twice a day. Side-effects were minimal. In 19 patients there was complete relief of symptoms, the ulcer crater being healed in 18. Of 15 similar patients given a placebo, only 4 had relief of symptoms, and in only one was there radiological evidence of healing of the ulcer. A follow-up investigation 1 to 18 months after treatment revealed that symptoms had recurred in 7 of the 25 patients within 2 to 12 months; 5 of these 7 again responded well to a course of piromen, but 2 did not respond.

Piromen is recommended as an adjuvant in the treatment of duodenal ulcer. Work is in progress in which piromen is being used together with an antispasmodic and antacids. *Joseph Parness*

## LIVER

1626. **Observations on the General and Regional Anatomy of the Human Liver**
H. Elias. *Anatomical Record* [*Anat. Rec.*] **117**, 377–394, Nov., 1953. 17 figs., 6 refs.

In continuation of his study of the anatomy of the liver, carried out at Chicago Medical School, the author has examined 8 further human livers. It was confirmed, as previously shown, that the generally accepted anatomical description of the branches of the hepatic artery, portal vein, and bile ducts, one of each enclosed in a fibrous capsule and the whole forming the so-called portal triad, was not applicable to the whole liver. At the porta hepatis and for a varying distance into the liver no such portal triad existed. The branches of the portal veins showed a constant pattern throughout, but the branches of the hepatic artery and the tributaries of the bile ducts did not at first maintain a constant relation either to each other or to the portal veins. Only deeper in the liver substance did they assume the classic form of the portal triad enclosed in a fibrous capsule and entirely sur-

rounded by liver tissue, as first described by Francis Glisson in his *Anatomia hepatis* published in London in 1654.

A continuous plate of liver cells separating the liver parenchyma from Glisson's capsule is described. The left and quadrate lobes of the liver may be separated by connective tissue or they may be joined by liver parenchyma. The hepatic tissue is conventionally divided into para-portal, intermediate, and para-hepatic (central) zones, which are not normally distinguishable from each other. The para-hepatic zone invests the tributaries of the hepatic vein with a continuous coat and follows their branches. Intermediate zones separate the para-portal from the para-hepatic zones, but this zonal arrangement may be altered by changes in portal or hepatic blood pressure. *W. Skyrme Rees*

1627. **The Incidence of Residuals of Viral Hepatitis**
L. Zieve, E. Hill, S. Nesbitt, and B. Zieve. *Gastroenterology* [*Gastroenterology*] **25**, 495–531, Dec., 1953. 9 figs., bibliography.

In this paper from the Veterans Administration Hospital and University of Minnesota, Minneapolis, the authors present the results of an investigation into the incidence of cirrhosis of the liver as a long-term sequel to viral hepatitis. A total of 367 ex-servicemen were examined clinically, and a battery of eleven liver function tests (and in some cases liver biopsy) carried out. The men examined fell into three groups: (1) a " hepatitis " group of 367 subjects shown by U.S. Army and Veterans Administration records to have had viral hepatitis while in the service during the years 1942–5; (2) a " maximally exposed " group of 137 men who had been members of army divisional units with exceptionally high hospital admission rates for hepatitis (at least 263 per 1,000 men per year); and (3) a " control " group of 212 men who had never been exposed to epidemic or endemic hepatitis during their service and had no history of jaundice, liver disease, syphilis, malaria, yellow-fever vaccination, blood or plasma transfusion, or serious injury. Among the men in Group 1 there were 144 who had had serum hepatitis, practically all following yellow-fever vaccination; there were also 186 cases of " probable infectious hepatitis " and 26 of multiple attacks of hepatitis. Comparison of the results of those tests primarily measuring hepatocellular function showed there to be essentially no differences between the various groups, the occurrence of functional abnormalities among the men who had had viral hepatitis 4 to 6 years previously being no greater than would be expected in any similar group of healthy young males, and this conclusion was corroborated by the results of biopsy studies. The authors suggest that the results of their investigation are not inconsistent with those of previous studies in which a significantly high incidence of residual effects and recurrences has been found during the one- to two-year period immediately following an attack of acute hepatitis. Whereas the relatively high incidence of short-term sequelae has led previous investigators to anticipate a similarly high incidence of long-term effects, the present investigation indicates that time encourages healing rather than progression. Nor do these negative findings conflict with the observation in individual cases of a continuous transition from acute hepatitis to cirrhosis: they merely indicate that such cases are infrequent.

Although the incidence of functional or structural abnormalities of the liver was no greater among men who had had viral hepatitis than among those who had not, there did appear to be certain immunochemical sequelae of viral hepatitis which manifested themselves in abnormalities of the serum proteins or lipoprotein complexes, and in this respect the response to the infective hepatitis virus appeared to be more intense and prolonged than to the virus of serum hepatitis. Thus the average result of the zinc sulphate turbidity test was greater, and there were more abnormal thymol turbidity values, among the cases of infective hepatitis than among those of serum hepatitis or the control cases; the average serum cholesterol concentration was higher in Group 1 than in Group 2, but was approximately the same for cases of infective and serum hepatitis. On the other hand 58 out of 60 liver biopsy specimens from cases in Group 1 were normal, compared with 12 out of 16 from control cases. *E. Forrai*

1628. **Clinical Evaluation of the Hepatic Radioactivity Survey**
E. T. Yuhl and L. A. Stirrett. *Annals of Surgery* [*Ann. Surg.*] **138**, 857–862, Dec., 1953. 3 figs., 5 refs.

The results are reported of a " hepatic radioactivity survey " carried out on a series of 283 patients with malignant and non-malignant liver disease at the Veterans Administration Center, Los Angeles. The method used employs radioactive iodinated human albumin as a tracer substance, gamma radiation being detected with a scintillation counter. For reasons which are not yet clear, a high concentration of the tracer occurs in metastatic growth, above which the average radioactivity count is 30% greater than that above normal tissue, whereas primary neoplastic tissue shows no such selective concentration. It is thus possible in many cases to determine whether hepatic metastases are present, without subjecting the patient to operation. Unfortunately, however, the presence of intraperitoneal fluid or of inflammatory processes in the liver or elsewhere in the abdomen, such as active peptic ulcer, is likely to cause a false positive result, but false negative findings tend to occur only if the metastasis lies towards the back of the liver or is less than 2 cm. in diameter. Within these limitations the method appears to provide useful information.

Of 187 patients who had had proved primary growths but in whom no hepatic metastases had been found on laparotomy or biopsy, all but 6 gave negative results. Of 53 patients in whom metastases were found at operation, 49 gave a positive result; in only 11 of these cases were hepatic metastases suspected clinically, and in almost half of them liver function tests gave normal results.

[There is a type of case in which the information which this method appears to provide may be of real value, and this paper suggests that a useful new aid to diagnosis has been devised.] *Thomas Hunt*

# Cardiovascular System

1629. **Orthostatic Factors in Pulsus Alternans**
B. FRIEDMAN, W. M. DAILY, and R. S. SHEFFIELD. *Circulation* [*Circulation* (*N.Y.*)] **8**, 864–873, Dec., 1953. 5 figs., 13 refs.

At the Veterans Administration Hospital, McKinney, Texas, in the past 2 years the authors have observed in 3 patients with organic heart disease the occurrence of pulsus alternans which was closely related to posture, being most evident when the patient stood up and becoming modified or abolished by the patient's lying down, by exercise, or by digitalis. The electrocardiograms showed impulses of sinus origin of similar cycle-length and identical configuration for both strong and weak beats; electrical alternation was not observed. Clinically, the detection of pulsus alternans is facilitated if the patient is examined after being in a sitting or standing position for some minutes.

The authors believe that there are two principal factors involved in the causation of pulsus alternans: (1) a weakened or injured heart muscle which has insufficient contractile strength to empty the ventricle efficiently except under conditions of increased stretch; and (2) a precipitating extracardiac haemodynamic factor which exerts its effect by changes in the ventricular inflow and in peripheral resistance. *James W. Brown*

1630. **The Wave of Ventricular Activation in Left Bundle-branch Block with Infarction. (A New Electrocardiographic Sign)** (La onda de activación ventricular en el bloqueo de rama izquierda con infarto. (Un nuevo signo electrocardiográfico))
E. CABRERA and C. FRIEDLAND. *Archivos del Instituto de cardiología de México* [*Arch. Inst. Cardiol. Méx.*] **23**, 441–460, Aug. 31, 1953 (Received Jan. 1954). 7 figs., 8 refs.

The electrocardiographic signs of cardiac infarction are often masked if there is concurrent left bundle-branch block. In order to elucidate the electrocardiographic signs of the combined lesion, the authors reviewed all cases of complete left bundle-branch block seen at the National Institute of Cardiology, Mexico City, during a period of 9 years, from which 45 cases were selected for this study. The clinical findings, electrocardiograms (ECGs), and post-mortem findings, if available, were correlated and the cases classified according to whether or not infarction was present.

In 11 cases there was definite infarction and in 10 of these the ECG showed a notch lasting 0·05 second or more in the terminal portion of QRS in those precordial leads having a morphology rS or QS; interpretation of the ECGs by classic methods would have revealed only 8 cases. In 5 of the cases examined at necropsy the infarct was antero-septal. Of the 34 cases of left bundle-branch block not complicated by infarction, in only 2 was the notch present consistently. In 22 of the 34 cases without infarction, VL was recorded. Taking the aforementioned notch as a criterion, the possibility of misdiagnosis was 9%; judged by the presence of a Q wave in Lead I the possibility was also 9%; but judged by the Q wave in VL it was 32%. If any two of the above three criteria were considered as essential to diagnosis, the maximum possible chance of diagnosing an infarct when none was present was 1 in 34. In cases of complete left bundle-branch block the presence of the notch described gives a probability of an infarct being found of 83%. The notch is not observed in septal infarcts without left bundle-branch block.

The study did not include cases of infarct not involving the septum or of infarct of the diaphragmatic surface; these, it is suggested, may be more difficult to diagnose. The mechanism of production of the notch is not yet certain, but two hypotheses are advanced: (1) that there is a focal block; or (2) that there is interpolation of an area of inactive tissue located in the septum or in the paraseptal portion of the anterior wall. The relative merits of these two hypotheses are discussed, and a number of illustrative ECGs are presented.

*D. Goldman*

## CONGENITAL HEART DISEASE

1631. **Surgical Closure of Atrial Septal Defects**
R. E. GROSS and E. WATKINS. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **67**, 670–685, Nov., 1953. 10 figs., 4 refs.

The authors, writing from Harvard Medical School, review the various surgical techniques now employed in the treatment of atrial septal defects. They state that in principle these fall into four main groups. (1) Repair under direct vision, employing some form of artificial circulation or refrigeration and temporary arrest of the circulation. (2) Suture of the auricular wall itself to the margin of the defect. (3) " Blind " suture of the anterior edge of the defect to the posterior auricular wall. (4) Suture of some inert material such as polyethylene directly to the edges of the defect, using the principle of the atrial well as described by the authors (*New Engl. J. Med.*, 1952, **247**, 455; *Abstracts of World Medicine*, 1953, **13**, 213).

In the authors' experience Method 3 is ideal for high posterior and small defects and Method 4 is the best for larger and anterior lesions, but as yet no completely adequate method has been devised to deal with the large, low, anterior defects which have no edges and which abut on the tricuspid valve. They mention the not uncommon association of anomalous pulmonary venous drainage with atrial septal defects, and stress the importance of the correction of this lesion. Of 12 of the authors' patients treated by Methods 3 and 4, 5 died as a result of the operation, but all 7 survivors had considerable

subjective improvement and 3 out of 4 of these who were examined by cardiac catheterization after operation showed no evidence of any interatrial shunt.

The authors go on to discuss the selection of cases for these operations and state that, as bacterial endocarditis is rare in this condition, fear of future development of this condition does not justify operation, but that the only indication for surgery is the increased work thrown on the right ventricle and the inherent likelihood of its eventual failure. They recommend that only patients with large shunts should be subjected to operation—they have adopted the arbitrary rule that where the right ventricular output is double that of the left ventricle, operation should be undertaken. The best age for operation is between 4 and 30 years of age. In their view right heart failure is not a contraindication to surgery, but high pulmonary arterial pressure due to associated organic changes in the arterioles renders operation hazardous. *J. R. Belcher*

1632. **The Tetralogy of Fallot. I. Embryology and Morbid Anatomy. Operative Technique and Analysis of 19 Cases Treated by Brock's Operation.** (La tetralogia di Fallot. I. Considerazioni embriologiche ed anatomopatologiche. Tecnica operativa ed analisi di 19 casi sottoposti all'operazione di Brock)
M. A. CHIECHI. *Chirurgia toracica* [*Chir. torac.*] **6**, 277–304, Aug.–Oct., 1953. 12 figs., 37 refs.

In this paper from St. Michael's Hospital, Newark, New Jersey, the author discusses the embryology, morbid anatomy, and surgical treatment of the tetralogy of Fallot, the most common of the congenital cardiac malformations. He favours Spitzer's philogenic theory to explain the embryological basis of the tetralogy. This postulates that in the evolution of the heart a "distortion" occurs, resulting in transposition of the great vessels; there is a partial rotation affecting only the aorta, which is dextraposed so that it overrides the ventricular septum and arises in part from the right ventricle, thus causing an augmented aortic flow with a corresponding deficiency in the pulmonary circulation. The degree and extent of these malformations can vary greatly, from an extreme degree of pulmonary atresia to only slight aortic displacement. The different anatomical types are discussed at length, and the significance of the resulting obstruction to the pulmonary outflow is studied with reference to operation on the living subject. Pulmonary outflow obstruction may be due to: (1) a pure valvular stenosis; (2) pulmonary infundibular hypoplasia, a bicuspid valve, and a subvalvular stenosis; (3) subvalvular stenosis at the infundibular orifice, with the formation of a third ventricle, beyond which a relatively normal valve may or may not be present. About 40% of cases are due to pure valvular obstruction.

A critical appraisal of the Blalock–Taussig operation is made. The direct opening up of the stenotic valve by Brock's method is considered a more rational method; in cases of extreme pulmonary infundibular hypoplasia, however, no direct relief of the obstruction is possible, and then an anastomotic operation must be performed. Some modifications of the direct Brock operation introduced by Glover *et al.* are described. Of 19 patients subjected to the operation, 8 had valvular stenosis, 9 infundibular stenosis, and 2 supravalvular stenosis of the pulmonary artery. There were 4 immediate postoperative deaths and another patient died 3 months later from cardiac failure, a mortality of 26%. The main postoperative complication was a marked increase in respiratory rate.

[It appears from the author's second paper (see Abstract 1633) that one more patient has since died, making the mortality 31%.] *C. A. Jackson*

1633. **The Tetralogy of Fallot. II. Results of Brock's Operation in 19 Cases Followed up for 6 to 24 Months.** (La tetralogia di Fallot. II. Interpretazione dei risultati di 19 casi operati secondo il metodo di Brock e seguiti da sei mesi a due anni)
M. A. CHIECHI. *Chirurgia toracica* [*Chir. torac.*] **6**, 305–337, Aug.–Oct., 1953. 7 figs., bibliography.

Among the 19 patients described above (Abstract 1632) undergoing operation for the tetralogy of Fallot there were 4 operative deaths and 2 other patients died later. Of the 13 survivors, the results were classified as "excellent" or "good" in 6 and "mediocre" or "poor" in 7. The criteria of immediate postoperative success were the disappearance of the cyanosis, increased exercise tolerance, and a return to normal haematocrit values. In 4 of the 7 less satisfactory cases there was radiological evidence of slow cardiac enlargement with augmented pulmonary vascular shadows, indicating progressive heart failure.

The author comes to the conclusion that the essential factors contributing to failure are a large interventricular defect and marked overriding of the aorta, that the pulmonary stenosis is in fact a defence mechanism protecting the lungs from the full effects of hypertension, and that when a successful valvotomy has been performed irreversible changes develop in the pulmonary vascular bed, causing the increasing resistance to which must be attributed the attendant symptoms of dyspnoea and cardiac failure. Thus in effect the stenosis has been transferred to the peripheral pulmonary vessels (Eisenmenger complex). Since the better results followed a less successful correction of the stenosis, the value of the operation must yet remain to be decided.

[This interesting analytical study gives later follow-up results for many of the cases previously described in the paper by Glover *et al.* (*J. thorac. Surg.*, 1952, **23**, 14; *Abstracts of World Medicine*, 1952, **12**, 128).]
*C. A. Jackson*

1634. **Anatomic Variations in the Tetralogy of Fallot**
T. G. BAFFES, F. R. JOHNSON, W. J. POTTS, and S. GIBSON. *American Heart Journal* [*Amer. Heart J.*] **46**, 657–669, Nov., 1953. 10 figs., 10 refs.

In an attempt to determine the relative merits and dangers of a direct approach to the pulmonary valve with infundibular resection and of creation of a shunt between the subclavian and pulmonary arteries in the treatment of Fallot's tetralogy, 350 post-mortem specimens showing congenital deformities of the heart from a collection made at the Children's Memorial Hospital,

Chicago, were critically reviewed and 42 selected which fulfilled the criteria of tetralogy of Fallot. There were 12 with pulmonary atresia, in 4 of which the pulmonary arterial segment was adequate for a shunt operation. Of the remaining 30 hearts, all had infundibular stenosis, and 10 had valvular stenosis as well. The amount of overriding was less than 25% in 5 cases, between 25 and 50% in 18 cases, and over 50% in 7 cases.

In 8 instances (27%), the stenosis was caused by a thin fibro-muscular band at the lower bulbar orifice and could have been relieved by infundibular resection. In the other 22 cases, however, infundibular resection would have been a formidable procedure. The various kinds of stenosis encountered were classified: the commonest was tubular and involved the whole infundibulum. The authors admit that hearts fixed in formalin may give a false impression of their physiological behaviour; they also point out that the great majority of the hearts studied came from children under 3 years of age, whereas most previously published studies of a similar nature in which the findings have differed from theirs have been carried out on older children and adults. *Paul Wood*

## CHRONIC VALVULAR DISEASE

1635. **The Clinical Diagnosis of Thrombosis of the Left Auricular Appendage.** (Sulla diagnostica clinica della trombosi auricolare sinistra)
V. NAZZI. *Cuore e circolazione* [*Cuore e Circol.*] **37**, 193–205, Aug., 1953 [Received Dec., 1953]. 11 figs., bibliography.

The presence of intracardiac thrombosis is rarely recognized from clinical signs, and with the exception of those cases in which calcified thrombi are visible radiologically the diagnosis is usually established by the occurrence of embolic phenomena.

It is possible, however, in some cases, to diagnose the condition during life when the thrombosis occurs in the left auricular appendage, which is the site of election in mitral stenosis with auricular fibrillation, and the author describes two such cases.

In the first a patient with mitral stenosis and auricular fibrillation showed the typical *x*-ray appearances of a " mitral heart ", with shallow and irregular contractions of the ventricles and dilatation and absence of pulsation of the third left arch (between the pulmonary artery and the left ventricle) on kymography. After quinidine had been given the ventricles showed regular deep contractions, but the third left arch was still immobile, although jugular phlebograms and oesophago-atriograms showed there to be mechanical contraction of both atria. These findings strongly suggested the presence of thrombosis of the left auricular appendage, which in mitral valvular disease, and especially when enlarged by thrombosis, is visualized on the left border between the pulmonary artery and the left ventricle; this is partly due to the enlarged right ventricle causing a clockwise rotation of the heart on its long axis.

A second patient with similar radiological appearances died suddenly a few days after admission. At necropsy the left atrium was very dilated and its appendage, which was double the normal size, was lined with thrombus, which was separating.

The importance is stressed of the establishment and maintenance of sinus rhythm with adequate doses of quinidine and of anticoagulant therapy in cases of mitral disease. *W. D. Nichol*

1636. **Mitral Stenosis and Cor Pulmonale**
A. C. TAQUINI, B. B. LOZADA, R. J. DONALDSON, R. E. H. D'AIUTOLO, and E. S. BALLINA. *American Heart Journal* [*Amer. Heart J.*] **46**, 639–648, Nov., 1953. 4 figs., 9 refs.

The authors point out that amongst cases of mitral stenosis there are a few which follow a rapid downhill course with early signs of right ventricular strain and congestive heart failure. In 30 such cases which were studied at the University of Buenos Aires the outstanding symptom was dyspnoea, often with paroxysms of asthmatic breathing and frequent haemoptyses. They constituted about 5% of all cases of rheumatic heart disease seen. The electrocardiographic and *x*-ray appearances suggested marked pulmonary hypertension, and the pulmonary arteriolar resistance was very high in the 3 cases in which it was measured.

*Paul Wood*

1637. **Valvotomy in the Treatment of Mitral Stenosis**
T. HOLMES SELLORS, D. E. BEDFORD, and W. SOMERVILLE. *British Medical Journal* [*Brit. med. J.*] **2**, 1059–1067, Nov. 14, 1953. 5 figs., 17 refs.

The basic indications for operation in mitral stenosis are: (1) the stenosis must be severe and of a type suitable for surgical correction; (2) the symptoms must be disabling enough to warrant the risks of surgery; and (3) the symptoms must be entirely or mainly due to mitral obstruction. In the authors' opinion, suitability for operation " will usually be decided on the basis of routine cardiological examination rather than on catheter findings ". Operability of the lesion must first be determined, the type of stenosis most suitable for surgical correction being the " diaphragmatic valve ", in which the two cusps are fused but still remain pliant and mobile, although their margins may be thickened. The physical signs suggesting mobility are: (1) a snapping first sound at the apex; (2) a " tapping " apex beat; and (3) an " opening snap " or sharp click which closely follows the second sound and is best heard a little inside the apex. The next most important consideration is the degree of permanent myocardial damage present, the best measure of which is given by the size of the right ventricle. Cases in which the stenosis is considered to be operable may be classified as follows: (I) with minimal or no signs of right ventricular enlargement; (II) with considerable right ventricular enlargement but without congestive heart failure; and (III) with gross ventricular enlargement and congestive failure.

Out of a total of 150 patients treated by valvotomy—87 at the Middlesex Hospital, London, and 63 at Harefield Hospital and the London Chest Hospital—there were 4 operative and 4 later deaths; in 81 (74%) out of 111 cases in which the follow-up period was adequate the results were regarded as " good ". From a study of

this series the authors conclude that the pulmonary arterial pressure does not provide an accurate indication of the degree of mitral stenosis present, the size of the right ventricle giving a better idea of the cumulative effect of pulmonary hypertension on the heart. Whether it is due to rheumatic myocardial damage or the mechanical effect of a defective valve, gross enlargement of a ventricle is unlikely to be reversible, but surgery is not contraindicated if there are signs that the valve is pliable. The presence of auricular fibrillation alone should not influence the decision to operate and does not affect the results; most of the authors' cases with sinus rhythm were digitalized before operation, but fibrillation developed at or soon after valvotomy in 25%. Operative and postoperative emboli occurred in 9 instances; 5 of these patients died, 2 have permanent hemiplegia, and 2 only have recovered. While free mitral incompetence and tricuspid stenosis or incompetence are contraindications to mitral valvotomy, slight degrees of aortic stenosis or incompetence can be ignored in cases where the mitral stenosis is the dominant lesion.

The problems arising from the association of pulmonary complications, such as chronic bronchitis and emphysema, and of pregnancy with mitral stenosis are also discussed, as are features of operative technique.

[There is a lot of good, sound, practical advice in this article, to which no abstract can do justice. It should be carefully studied in the original by all who have such patients under their care.] *W. P. Cleland*

1638. **Electrocardiographic Findings in Mitral Stenosis in Relation to the Operation of Commissurotomy.** (Il quadro elettrocardiografico della stenosi mitrallica in rapporto all'intervento di commissurotomia)
G. MAGRI and E. JONA. *Minerva medica* [*Minerva med. (Torino)*] **2**, 1709–1717, Dec. 5, 1953. 1 fig., 42 refs.

The electrocardiographic findings in 20 patients were studied at the University Cardiac Clinic, Turin, before, and one month and 6 months after, valvotomy for mitral stenosis. All these patients were in sinus rhythm. Significant changes occurred in the P waves only, which before operation were of the "mitral" type. In 15 cases the P waves became more normal in appearance after surgery, but in 5 of them reversion to the original pattern later took place. In 2 of the other 5 patients in whom no improvement was observed the stenosis reformed following postoperative rheumatic fever.

[The findings in this small series are somewhat inconclusive.] *D. Weitzman*

1639. **A Phonocardiographic Study of Mitral Stenosis in Relation to the Operation of Commissurotomy.** (Studio fonocardiografico della stenosi mitralica in rapporto con l'intervento di commissurotomia)
G. MAGRI and P. PINNA-PINTOR. *Minerva medica* [*Minerva med. (Torino)*] **2**, 1717–1728, Dec. 5, 1953. 9 figs., 20 refs.

At the University of Turin, the phonocardiographic findings in 34 patients with mitral stenosis were compared before and after valvotomy. After operation an opening snap was recorded in 30 patients (88%), occurring at 0·06 to 0·14 second after the beginning of the second sound; it eventually returned to its preoperative amplitude. The mitral diastolic murmur disappeared or diminished in intensity in 21 cases (63%) shortly after operation, but later tended to return to the original amplitude. A presystolic bruit, which was recorded preoperatively in 25 of the 26 cases in sinus rhythm, persisted after surgery in 16, although with diminished amplitude. Systolic murmurs were recorded preoperatively in 27 patients. In 3 of these it was pan-systolic and these patients were considered to have a mitral reflux at operation; in the remaining 24 cases it was considered to be of either aortic, tricuspid, or "functional" [*sic*] origin. Its amplitude tended to increase after surgery.

*D. Weitzman*

## CORONARY DISEASE AND MYOCARDIAL INFARCTION

1640. **Myocardial Infarction and its Treatment with Anticoagulants. Summary of Findings in 1,031 Cases**
I. S. WRIGHT, D. F. BECK, and C. D. MARPLE. *Lancet* [*Lancet*] **1**, 92–95, Jan. 9, 1954. 15 refs.

In 1946 the American Heart Association set up a committee to determine the value of anticoagulants in the treatment of myocardial infarction, a preliminary report, based on the first 800 cases, being published in 1948 (*Amer. Heart J.*, **36**, 801; *Abstracts of World Medicine*, 1949, **6**, 187). In the present paper the authors summarize the findings in a total of 1,031 cases treated at 16 different centres in the U.S. over a period of 2 years.

Dicoumarol was given to 589 patients and the results of this treatment were compared with those obtained in 442 patients receiving "conventional" therapy only. The more important findings were as follows. Of the 442 patients in the control group 23·4% died within 6 weeks compared with 16% of the treated group. During the period of effective anticoagulant therapy—that is, from the fourth day of treatment to 4 days after the last dose of dicoumarol—9·5% of the treated patients died, whereas 17·4% of the untreated patients died during the corresponding period. During a 6-week observation period thrombo-embolic complications developed in 26% of the control group but in only 11% of the treated group. Mural thrombi were found in the heart in two-thirds of the control patients and one-third of the treated patients coming to necropsy. A significant reduction in the incidence of thrombo-embolic complications in treated patients was achieved when the prothrombin time was prolonged to at least 25 to 39 seconds; prolongation beyond this range resulted in no additional benefit. It is concluded that to confine anticoagulant therapy in myocardial infarction to the more seriously ill patients is not justified.

[Many will remain unconvinced that the case has yet been fully proved for administration of anticoagulant drugs in all cases of myocardial infarction when specific contraindications are absent. The promised publication of a full account of this important work will be awaited with interest.] *Bernard Isaacs*

1641. **The Association between Hypoglycaemia and Myocardial Infarction**
B. GANDEVIA. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 33–36, Jan. 9, 1954. 15 refs.

By studying two series of cases the author, at the Royal Melbourne Hospital, Melbourne, attempted to assess the frequency of the association between hypoglycaemia and myocardial infarction.

Of 50 consecutive patients with myocardial infarction, 6 had had an antecedent hypoglycaemic reaction at approximately the time of onset of the infarction. Five of the patients were diabetics who had been receiving insulin for some years, and the sixth had an islet-cell tumour of the pancreas. Further support for the view that hypoglycaemia bears more than a casual relationship to cardiac infarction was found in an analysis of the cause of death in 55 diabetic patients coming to necropsy. In 14 of these there was evidence of myocardial infarction, 6 of the 14 having had a hypoglycaemic reaction at approximately the time of onset of the infarction. Of the 41 patients in whom death was due to other causes, only 4 had had a hypoglycaemic attack which might have been connected with death.

Discussing the possible mechanism by which hypoglycaemia could cause cardiac infarction and anginal pain, the author suggests that they are most likely the result of a hyperdynamic circulatory state. Other workers have shown that this state, with abnormal changes in the electrocardiogram, may persist after the blood sugar level has returned to normal. The changes are, however, inhibited by administration of neostigmine and abolished by combined denervation of the heart and adrenalectomy, but not by either procedure alone. It is therefore suggested that the development of angina or myocardial infarction in hypoglycaemia is an expression of increased cardiac work in the probable presence of some coronary sclerosis. A high-protein diet is recommended as a prophylactic in patients who have any anginal symptoms associated with hypoglycaemia. The importance of preventing hypoglycaemic reactions in elderly diabetic patients with a diminished cardiac reserve is emphasized and it is suggested that small doses of neostigmine should be given as a prophylactic in hypoglycaemic attacks.

*J. Lister*

1642. **Survival Rates after Myocardial Infarctions with and without Long Term Anticoagulant Therapy**
J. W. KEYES, E. H. DRAKE, T. N. JAMES, and F. J. SMITH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **226**, 607–610, Dec., 1953. 4 refs.

Some 60 selected patients at the Henry Ford Hospital, Detroit, received dicoumarol therapy for long periods after the acute phase of myocardial infarction, the survival rate in this group being compared with that in a larger control group receiving no anticoagulant after the acute phase. From a statistical analysis of the results the authors conclude that the prognosis over a 1- to 2-year period was better in the treated group than in the control group. [The " levels of significance " accepted for this conclusion were not strict, the follow-up investigation does not appear to have been completed, and the long-term administration of dicoumarol, as the authors point out, was not without hazard.]

*W. J. H. Butterfield*

1643. **Influence of Various Alcoholic Beverages on Coronary Flow. Experiments on Isolated Rabbit Hearts.** [In English]
O. VARTIAINEN, E. V. VENHO, and M. VAPAAVUORI. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **42**, 162–173, 1953. 11 figs., 14 refs.

In experiments carried out at the University of Helsinki the effect of pure ethyl alcohol and various kinds of aromatic alcoholic drinks on the coronary blood flow was measured in isolated rabbits' hearts. Ethyl alcohol caused but little coronary vasodilatation; old aromatic brandies on the other hand increased the flow by 10 to 15%. There may be some justification, therefore, for encouraging patients with angina pectoris to take a little old brandy [if they can afford it].

*Paul Wood*

## HEART FAILURE

1644. **Clinical Evaluation of Gitalin in the Treatment of Congestive Heart Failure**
S. P. DIMITROFF, G. C. GRIFFITH, M. C. THORNER, and J. WALKER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 1189–1199, Dec., 1953. 12 refs.

The cardiac glycoside, gitalin, was first isolated from *Digitalis purpurea* by Kraft 40 years ago. Renewed interest has been taken in the drug with the introduction of an amorphous form which is both stable and uniform, is as effective as other glycosides for the induction and maintenance of adequate digitalization, and is one-third less toxic than digitalis leaf, digitoxin, or digoxin.

At the Los Angeles County Hospital gitalin was tried in the treatment of 68 patients with congestive cardiac failure, including 8 in whom digitalis, digitoxin, and digoxin were ineffective because of toxicity. The average dose for digitalization was about 6·0 mg. by intravenous injection, 6·5 mg. orally by the rapid method (1 mg. every 4 or 6 hours), and 7 mg. orally by the slow method (1·5 mg. daily for 4 to 6 days). The normal maintenance dose was 0·5 mg. daily. The drug was safe and effective for the initial digitalization and for maintenance, no toxic effects being encountered in this series. The authors state that when a toxic state is induced with gitalin the effects are similar to those of other preparations but the duration is much shorter.

*T. Semple*

1645. **The Failure of Hypertonic Saline in the Treatment of Hyponatremia and Edema in Congestive Heart Failure**
J. F. URICCHIO and D. G. CALENDA. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 1288–1294, Dec., 1953. 2 figs., 6 refs.

Hyponatraemia with oedema in congestive heart failure is almost invariably fatal. The onset may be insidious—chronic dilution hyponatraemia—or acute—the so-called low-salt syndrome. In most cases the condition develops rapidly after intensive mercurial therapy and may be accompanied by mental aberration,

anorexia, nausea, vomiting, abdominal cramps, nitrogen retention, and peripheral vascular collapse.

At Rhode Island Hospital, Providence, the present authors found that infusion of hypertonic saline in such cases was ineffective. Although the electrolyte concentration became normal in some cases, the infusion had no effect on oedema and did not produce diuresis. If mercurial diuretics were given when the serum sodium concentration became normal there was prompt diuresis, but this was followed by a recurrence of hypotonicity and oedema. In most instances, the patient developed intolerable thirst during the saline infusion and demanded water; he thus became " more waterlogged and more saltlogged and still showed evidence of hypotonicity ".

The authors conclude that this method of treatment is invariably ineffective and may lead to aggravation of the patient's condition. All 7 patients in this series died.

*T. Semple*

1646. **Unrecognized Emboli to the Lungs with Subsequent Cor Pulmonale**

W. R. OWEN, W. A. THOMAS, B. CASTLEMAN, and E. F. BLAND. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 919–926, Dec. 3, 1953. 5 figs., 35 refs.

It is well known that pulmonary embolism may occur without being recognized clinically. If the emboli are widespread they ultimately cause serious obstruction to the pulmonary blood flow with an increased burden on the right ventricle, leading to cor pulmonale. In 8,000 consecutive necropsies at the Massachusetts General Hospital, Boston, the authors found 12 cases of cor pulmonale due to pulmonary hypertension from this cause. The characteristic clinical picture was of increasingly severe congestive heart failure with normal rhythm in the absence of any determinable cause; haemoptysis was uncommon. Dyspnoea and cough were the most frequent symptoms. One patient had a left recurrent laryngeal nerve palsy from pressure of the distended pulmonary artery. Syncope was encountered in one case only. Cyanosis was a constant finding, but polycythaemia and clubbing of the fingers were infrequent. Gallop rhythm and accentuation of the second pulmonary heart sound were usual, and ascites was common. Radiologically, the lung fields were relatively ischaemic and clear, though the root vessels were prominent; infarcts were rarely seen. The electrocardiogram showed right ventricular hypertrophy, but no evidence of right bundle-branch block. Pathologically, the changes in the pulmonary vessels were identical with those produced in experimental animals by injection of various substances into peripheral veins, changes indistinguishable microscopically from localized arteriosclerosis. In the authors' view these findings suggest that many cases of the so-called Ayerza's syndrome result from latent embolization of the lungs. In these 12 cases repeated sub-clinical embolism from peripheral venous thrombosis was a more important aetiological factor than primary pulmonary thrombosis, for which the evidence was not conclusive.

*J. L. Lovibond*

## PERIPHERAL ARTERIES

1647. **Studies on Necrotizing Angiitis. IV. Periarteritis Nodosa and Hypersensitivity Angiitis**

H. C. KNOWLES, P. M. ZEEK, and M. A. BLANKENHORN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 789–805, Dec., 1953. 30 refs.

The authors have analysed the clinical and necropsy findings in 45 patients dying from necrotizing angiitis at the Cincinnati General Hospital. They deprecate the use of the term periarteritis nodosa for a heterogeneous group of disease conditions, and distinguish at least five different categories. In this paper they discuss the first three of these, namely, (1) primary periarteritis nodosa, in which the nodular vascular lesions, as first described by Kussmaul and Maier, are unassociated with any other major disease (14 patients); (2) secondary periarteritis nodosa, in which the nodular lesions develop shortly before death in patients suffering from severe renal disease with hypertension (21 patients); (3) angiitis associated with hypersensitivity to serum, sulphonamides, or other drugs (10 patients).

The most striking clinical differences were as follows. (1) Primary periarteritis nodosa was commoner in males, lasted several months with remissions and exacerbations, and at necropsy showed lesions at all stages of development. (2) The clinical findings in secondary periarteritis nodosa were masked by those of the renal disease with hypertension. In most cases the lesions had been initiated shortly before death and the diagnosis was made at necropsy. Gross haematuria with malignant hypertension was a common feature. (3) Hypersensitivity angiitis was a fulminating, febrile illness, rapidly fatal, often associated with the administration of sulphonamides, and characterized by rashes, nephritis, and myocarditis.

[This important article includes a great deal of matter which does not lend itself to abstracting, and those who are interested should read the original paper.]

*Arthur Willcox*

1648. **Intermittent Claudication of the Hip and the Syndrome of Chronic Aorto-iliac Thrombosis**

V. G. DEWOLFE, F. A. LEFEVRE, A. W. HUMPHRIES, M. B. SHAW, and G. S. PHALEN. *Circulation* [*Circulation (N.Y.)*] **9**, 1–16, Jan., 1954. 6 figs., 34 refs.

The authors believe that it is not generally realized that intermittent claudication can occur in sites other than the calf. The present report from the Cleveland Clinic, Cleveland, Ohio, is concerned with its occurrence in the hip, buttock, or occasionally the lower part of the back of 47 patients with arterial occlusion at the lower end of the aorta or in the iliac arteries, the common iliac artery being the vessel most commonly affected. The syndrome occurs predominantly in men between the ages of 40 and 60, and is seldom associated with trophic changes in the limbs because of the rich collateral circulation through the lumbar and sacral vessels, although pulsation in the legs may often be absent. Extreme fatigue of the lower limbs, wasting of the muscles, and

impotence may occur, but are much less frequent symptoms than claudication. In many of the cases described the condition had been diagnosed as osteoarthritis, bursitis, or prolapsed intervertebral disk. Aortography, the technique of which is described in some detail, is of great value both in diagnosis and in locating the site of occlusion.

Operative treatment has not proved very satisfactory; bilateral sympathectomy gives the best results at present, although arterial grafts may prove of greater value in the future. In the authors' experience with a group of 29 patients treated conservatively, only 3 have become worse. In their view, the belief that this is a progressive disease resulting in gangrene or occlusion of the renal arteries appears to be ill-founded. *A. Paton*

1649. **Sympathectomy for Atherosclerosis. Preliminary Heating Test**

P. H. DICKINSON and D. N. WALDER. *Lancet* [*Lancet*] **1**, 75–77, Jan. 9, 1954. 5 figs., 4 refs.

The object of the investigation described in this paper from the Royal Victoria Infirmary, Newcastle upon Tyne, and the University of Durham was to ascertain whether the results of the distant heating test were of any value in determining the probable outcome of sympathectomy in patients with intermittent claudication due to atherosclerosis. The test was applied to 34 legs of 28 patients over 45 years of age with intermittent claudication as the presenting symptom. The rise in skin temperature of the great toe of the affected limb brought about by immersing one arm in water at 45° C. was measured under standard conditions. The response to the test was considered " good " if there was a rise of 5° C. or more (21 legs); " fair " if there was a rise of between 1° and 5° C. (5 legs); and " poor " if the rise was less than 1° C. (8 legs). Patients were seen one year after sympathectomy had been performed and classified as " improved "—that is, the patient could walk at least twice the preoperative distance before experiencing pain in the limb—or " not benefited ". [It is not stated how the walking distance was determined.] In 13 of the 34 limbs the condition was " improved ". No statistically significant correlation ($P>0{\cdot}1$) was found between the results of the test and the clinical condition of the patient one year after sympathectomy. In 2 instances there was improvement after sympathectomy although the response to the heating test had been " poor ". *C. J. Longland*

1650. **Investigation of Obliterative Arterial Disease of the Lower Limb**

D. MESSENT, R. E. STEINER, and J. F. GOODWIN. *Lancet* [*Lancet*] **2**, 1324–1329, Dec. 26, 1953. 5 figs., 17 refs.

At the Postgraduate Medical School of London various methods of investigating the peripheral circulation in the lower limb were compared and evaluated. More than 100 patients with arterial disease of the lower limbs were studied, oscillometry being carried out with the Pachon oscillometer, skin blood flow estimated by skin temperature recordings, plethysmography, and determination of the fluorescein circulation rate, and calf blood flow estimated by plethysmography. The results were analysed and the value of each investigation was considered in relation to the arteriographic and clinical findings.

It is concluded that oscillometry, which reveals nothing but the upper level of arterial obstruction, is of no value in determining the degree or severity of ischaemia distal to the block and provides no guidance as to treatment or prognosis. It may possibly be of value sometimes in deciding the level of an amputation.

Tests of vasomotor release, such as skin temperature recording, foot plethysmography, and determination of the fluorescein circulation rate, provide some information about the maximum blood flow obtainable under experimental conditions, but are of little value in the assessment of the pathological condition present or in deciding for or against any form of surgical treatment. Measurement of the calf blood flow similarly yields no information of clinical value, but does give a better idea of the total blood supply to the limb.

In the authors' opinion arteriography is the only method which enables the investigator to recognize early disease, to locate accurately the anatomical lesion, and to visualize the collateral blood supply. It is an essential preliminary to any local surgical procedure, and a useful preliminary to amputation. A careful history and physical examination will provide a better guide to treatment than any method of special investigation, but if additional information is required, then arteriography is the method of choice.

[The original paper is full of information useful to workers in this field.] *Peter Martin*

## HYPERTENSION

1651. **Phrenic or Postemphysematous Hypertension**

C. F. GESCHICKTER and A. POPOVICI. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 767–788, Dec., 1953. 12 figs., 13 refs.

The authors call attention to the importance of pulmonary factors, especially emphysema, in the development of hypertension in middle age. They found that of 75 asthmatic patients over 40 years of age seen at Georgetown University Medical Center, Washington, D.C., 60 had emphysema [the criteria for the diagnosis of emphysema are not given], and that 28 (46%) of the emphysematous subjects had hypertension (defined as a blood pressure greater than 160/90 mm. Hg), whereas the expected incidence of hypertension in persons of this age is 20 to 25%. They suggest that the reason for the development of hypertension in emphysema is that the increased intrapleural pressure which is present and may become positive causes a raised venous pressure, which in turn leads to venous congestion of the kidneys and reflex compensatory arteriolar spasm.

In order to confirm this hypothesis the authors have investigated the effect of increasing the congestion in the inferior vena cava by placing the subject in the recumbent lordotic position, lordosis being achieved by inserting a sand-bag under the lumbar spine, thus, it is claimed, compressing the inferior vena cava between the liver and the spine and thereby raising the pressure in the distal

part of the vena cava and so in the renal veins. (It is this mechanism which is thought to cause orthostatic albuminuria.) The effect of this manœuvre on the blood pressure was recorded at one-minute intervals for 5 minutes in 25 normal individuals, 22 patients with emphysema and hypertension, and 14 patients with osteoarthritis of the spine or spondylitis with hypertension. A rise of 15 mm. Hg in diastolic pressure was considered a positive result. It was found that the diastolic pressure rose by 15 mm. Hg or more in 4 of the 25 normal subjects, in 14 of the 22 with emphysema and hypertension, and in 9 of the 14 with osteoarthritis or spondylitis, and the authors suggest that these results support their thesis. They also investigated the effect of increasing the rate of blood flow in the inferior vena cava in two hypertensive dogs. Hypertension was first produced by wrapping the kidneys in cellophane, and when it was established a portacaval anastomosis was made which increased the rate of flow through the vena cava. The animals' blood pressure fell considerably in one to 2 months after performance of the portacaval shunt.

In 21 of the 60 patients with asthma and emphysema electrocardiography showed evidence of myocardial damage. The authors suggest that the raised intrathoracic pressure interferes with the coronary venous return to the right auricle and that the myocardial damage is caused by coronary venous congestion.

*Arthur Willcox*

1652. **The Results of Surgical Treatment in 117 Cases of Essential Hypertension.** (Résultats du traitement chirurgical de l'hypertension artérielle permanente d'après 117 cas)

R. FONTAINE and V. CHARDON. *Strasbourg médical* [*Strasbourg méd.*] **4**, 631–644, Dec., 1953. 2 refs.

1653. **Hexamethonium in the Treatment of Hypertension**

M. HARINGTON and M. L. ROSENHEIM. *Lancet* [*Lancet*] **1**, 7–13, Jan. 2, 1954. 4 figs., 15 refs.

Experience with hexamethonium bromide in the treatment of hypertension and the results obtained over a period of 2 to 3 years at University College Hospital, London, are described. It is pointed out that the disadvantage of oral administration is the great variation in the amount of the drug absorbed from the intestine. Subcutaneous injection is preferred, and treatment is restricted to cases of malignant hypertension and of severe hypertension accompanied by retinal changes, left ventricular failure, or incapacitating headaches. Moderate renal failure, with a blood urea level not exceeding 100 mg. per 100 ml., is not a contraindication to the use of hexamethonium, although smaller doses are given because of impaired excretion. The drug is contraindicated in patients with a recent history of coronary or cerebral thrombosis.

Of 62 patients referred for treatment, only 26 were found suitable, as judged by the blood-pressure response to a test dose of 25 mg. of hexamethonium bromide intravenously. Treatment started with a subcutaneous injection of 25 mg. three times a day; this was increased, if necessary and if the patient could tolerate it, to 250 mg. Blood pressure was considered to be effectively controlled if the diastolic pressure with the patient standing was 100 mm. Hg or less 3 hours after an injection; this was achieved in 16 out of the 22 patients treated for more than 3 months. The authors state that hexamethonium by intravenous injection has proved useful in such hypertensive crises as acute pulmonary oedema and encephalopathy.

*C. W. C. Bain*

1654. **1-Hydrazinophthalazine ("Apresoline") in the Treatment of Hypertensive Disease: a Clinical Trial with a Control Group**

D. H. MERRILL and K. KENYON. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **226**, 623–631, Dec., 1953. 2 figs., 13 refs.

The effect of "apresoline" (hydrallazine) on a group of 39 patients with hypertension was compared with that of a placebo on a similar group of 37 patients. All the patients were seen by the same observer at an out-patient clinic of the Los Angeles County Hospital, who recorded blood pressure at each visit with the same sphygmomanometer. In both groups the blood pressure fell, but there was a "more significant" hypotensive effect in the patients receiving hydrallazine than in those receiving the placebo. [Statistically, the claim for this effect of hydrallazine rested upon the application of Student's t-test to markedly "skewed" values; no correction was made for patients who did not continue to attend the clinic; and it is not clear whether the observer knew the treatment that was being given. The symptomatic relief afforded by hydrallazine and by the placebos appears to have been much the same.]

*W. J. H. Butterfield*

1655. **The Treatment of Hypertension with Hexamethonium and Hydrazinophthalazine ("Apresoline")**

R. B. CUBBERLY, L. L. WIESEL, and A. E. LAMB. *Brooklyn Hospital Journal* [*Brooklyn Hosp. J.*] **11**, 125–134, 1953. 5 figs., 26 refs.

The pharmacology of two hypotensive agents, hydrallazine ("apresoline") and hexamethonium, is discussed with special reference to their sites of action and to the complications which may follow their administration, and the authors then report the results of treatment of 42 cases of hypertension with these drugs. After a preliminary period of observation all patients were given hydrallazine in increasing doses, up to a maximum of 500 mg. daily, for 2 to 3 months. In addition, 18 of the patients who did not respond well to hydrallazine were given hexamethonium.

Of the 42 patients, who were treated as out-patients, 21 responded satisfactorily to hydrallazine and a further 6 showed marked improvement after receiving hexamethonium; 13 did not respond to the former drug, nor did 10 to the latter drug. No serious side-effects were observed owing, the authors believe, to careful dosage and to a thorough understanding of the pharmacology of these agents. In their view the use of hydrallazine and hexamethonium is a marked advance in the therapy of hypertension.

*Kathleen M. Lawther*

# Haematology

1656. **Treatment of Blood Disorders with A.C.T.H. and Cortisone**

PANEL OF THE MEDICAL RESEARCH COUNCIL ON THE HAEMATOLOGICAL APPLICATIONS OF A.C.T.H. AND CORTISONE. *British Medical Journal* [*Brit. med. J.*] **2**, 1400–1401, Dec. 26, 1953. 3 refs.

The results of administration of ACTH or cortisone to 65 patients with haematological disorders are summarized. The dosage varied from 80 to 100 mg. a day for ACTH and from 100 to 300 mg. a day for cortisone. Most patients were treated for 2 to 3 weeks, the total dosage varying from 1,000 to 3,000 mg. of ACTH and from 1,000 to 7,000 mg. of cortisone. A "complete" response was defined as one in which the clinical condition of the patient and the haematological findings "returned approximately to normal", and a "partial" response as one in which "there was improvement of lesser extent".

Three out of 10 patients suffering from idiopathic or secondary acquired haemolytic anaemia responded partially and 5 responded completely. The reaction to the antiglobulin (Coombs) test was negative in 3 patients, including the 2 who failed to respond. Treatment was given to 22 patients with purpura. Of 15 with idiopathic thrombocytopenic purpura, 10 responded favourably, but in 5 out of 6 patients with non-thrombocytopenic purpura treatment was ineffective. Of 24 patients with acute leukaemia of various types or reticulosis, only 5 responded, the response being complete in 2.

The effect of the hormones on other haematological disorders (9 cases) is briefly mentioned. The paper also contains the results of a follow-up examination of 88 patients given ACTH or cortisone in 1951 (*Brit. med. J.*, 1952, **1**, 1261; *Abstracts of World Medicine*, 1952, **12**, 428).

It is concluded that the best results are likely to be obtained in cases of acquired haemolytic anaemia and of idiopathic thrombocytopenic purpura, but that as the response is usually temporary, treatment over many months may be necessary. *J. V. Dacie*

1657. **Immunoleucopenia and Immunoagranulocytosis.** (Immunoleucopénies et immunoagranulocytoses)

S. MŒSCHLIN. *Revue d'hématologie* [*Rev. Hémat.*] **8**, 249–262, 1953. 10 figs., 17 refs.

The immunological mechanisms responsible for the eucopenia and agranulocytosis caused by amidopyrin, virus pneumonia, and certain other conditions are as yet incompletely understood, and the author here presents a review of experimental and other observations bearing on the subject. The agranulocytosis caused by amidopyrin must be due to destruction of the leucocytes in the peripheral blood rather than to a mechanism primarily affecting bone marrow, because neutropenia is marked within a few hours of the administration of the drug and recovery occurs within 24 hours; the life of the granulocyte is 2 days in the blood, but 8 days in the marrow.

If the blood of a patient, sensitive to amidopyrin, to whom 0·3 g. of amidopyrin has been administered 3 hours earlier is transfused into a normal recipient the latter rapidly develops leucopenia, which may be shown to be due to a leuco-agglutinin active only in the presence of amidopyrin.

Similarly the blood of a patient with virus pneumonia, who had developed anaemia, leucopenia, and thrombocytopenia, induced a leucopenia when transfused into a normal subject. Incomplete cold agglutinins were demonstrated in the patient's serum.

In guinea-pigs the serum of rabbits immunized against guinea-pig leucocytes produces a leucopenia due to agglutination of leucocytes and their filtration in the lung capillaries, while the repeated subcutaneous injection of the serum produces the changes seen in human agranulocytosis.

It is suggested that a drug may combine with protein to form an antigen to which the recipient develops antibodies. These antibodies are thought to attach themselves to the leucocytes, causing their agglutination in the presence of the antigen. Prolonged stimulation of the marrow thus occurs, with final exhaustion. On the basis of this theory, granulocytopenia may be classified as follows: (1) "immunoleucopenia"—due to agglutinins formed by the mechanism described above; (2) primary marrow inhibition by such agents as irradiation or benzol; and (3) obliteration of the bone marrow, as in myelosclerosis (leucoerythroblastic anaemia).

[An excellent review of a very important modern development.] *George Discombe*

1658. **The Initial Stages of Blood Coagulation**

R. BIGGS, A. S. DOUGLAS, and R. G. MACFARLANE. *Journal of Physiology* [*J. Physiol.* (*Lond.*)] **122**, 538–553, Dec. 29, 1953. 8 figs., 16 refs.

The authors have previously shown (*J. Physiol.*, 1953, **119**, 89) that blood collected by clean venepuncture without tissue contamination develops a thromboplastic activity on contact with a foreign surface which is more powerful than that of tissue thromboplastin, and that all the factors necessary for this system are present in a mixture containing platelets, normal serum, and citrated plasma deprived of prothrombin by adsorption on aluminium hydroxide. In the present paper they show that the activity of the plasma fraction is attributable to Factor V and to antihaemophilic globulin (the missing factor in haemophilia), and that of the serum to Factor VII and the Christmas factor. Normal serum contains no prothrombin, Factor V, or antihaemophilic globulin because these are used up during clotting; this suggests that Factor V and antihaemophilic globulin are sub-

strates, and that Factor VII and the Christmas factor are catalysts, in the reactions resulting in thromboplastin formation. Using preincubated combinations of these factors the authors studied the preliminary reactions preceding the formation of active blood thromboplastin, and they describe experimental evidence suggesting that the action of contact which initiates clotting may be on the Christmas factor and platelets. *A. Brown*

1659. **The Action of Thromboplastic Substances**
R. BIGGS, A. S. DOUGLAS, and R. G. MACFARLANE. *Journal of Physiology* [*J. Physiol.* (*Lond.*)] **122**, 554–569, Dec. 29, 1953. 8 figs., 13 refs.

When the term " thromboplastin " was first introduced it was used to describe a factor present in tissue extracts in the belief that this was the only substance other than calcium required for the rapid conversion of prothrombin to thrombin, and the term is still used in general reference to tissue extracts—the one in common use being a preparation of brain. The authors of this paper suggest that the term " thromboplastic activity " should be given a wider significance to cover the whole of the mechanism involved in the conversion of prothrombin to thrombin, whether that activity be derived from tissues or from the blood itself. Factors V and VII have been accepted previously as accelerators of prothrombin conversion—that is, entering the reaction after prothrombin conversion starts—but experimental evidence described by the authors provides support for the suggestion that these factors react with brain extract before prothrombin conversion begins and that brain extract therefore has no thromboplastic activity in itself, but becomes active only after interaction with Factors V and VII. Trypsin and Russell viper venom both accelerate blood coagulation, and experiments are described which suggest that they also require Factors V and VII for their activity to become complete. Soya-bean trypsin inhibitor, which is anticoagulant, appears to act by destroying formed thromboplastin before it has an opportunity to cause prothrombin conversion.

The authors have also studied the action of heparin and have shown that it inhibits the formation of blood thromboplastin in very high dilutions. This action is in addition to its interference with the thrombin–fibrinogen reaction. *A. Brown*

1660. **Experiences of Management and Treatment of Polycythaemia Vera Using $P^{32}$ as a Therapeutic Weapon**
J. D. ABBATT. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.*] **5**, 141–147, Oct., 1953. 3 figs., 6 refs.

The author, working in the Medical Research Council Radiotherapeutic Research Unit, Hammersmith Hospital, London, reports the results of intravenous injection of 5 to 7 mc. of radioactive phosphorus ($^{32}P$) in the treatment of 30 patients aged 37 to 82 years suffering from polycythaemia vera. When the patients were first seen the disease had been present for 6 months to 16 years. In 25 of the cases the follow-up period has been sufficiently long to permit an assessment of the results.

In 20 of these 25 patients there was complete remission of all signs and symptoms of polycythaemia and a normal blood picture for a period of at least 6 months, this response being obtained with a single injection of $^{32}P$ in 18 of them. A partial remission with full symptomatic relief was obtained in 4, but one patient failed to respond. The author found that the platelet count, which was determined by a modification of the Lempert–Kristenson direct-counting technique, was helpful in judging the response to $^{32}P$. A fall in the count to 50,000 platelets per c.mm. or less, irrespective of the pre-treatment value, was invariably followed by a full remission.

The author confirms the findings of other workers that the full effect of $^{32}P$ may not be apparent for as long as 4 months after the initial treatment.
*D. G. Adamson*

## ANAEMIA

1661. **Mediterranean Anemia. A Study of Thirty-two Cases in Thailand**
V. MINNICH, S. NA-NAKORN, S. CHONGCHAREONSUK, and S. KOCHASENI. *Blood* [*Blood*] **9**, 1–23, Jan., 1954. 5 figs., bibliography.

1662. **Oral Administration of $Co^{60}$ Vitamin $B_{12}$ to Normal Persons, Patients with Pernicious Anemia, and Subjects with Various Medical Disorders**
L. M. MEYER, A. BECERRA-GARCIA, A. GOLDMAN, and P. A. STERN. *Journal of Applied Physiology* [*J. appl. Physiol.*] **6**, 263–268, Nov., 1953. 6 refs.

The authors describe experiments in which they administered vitamin $B_{12}$ containing radioactive cobalt ($^{60}Co$) by mouth to normal subjects, patients with pernicious anaemia, and patients with a miscellaneous group of medical disorders, the excretion of $^{60}Co$ in the stools being then measured. Whereas normal subjects excreted 8 to 41% of the dose administered (1 $\mu$g.), patients with cardiac disease, cirrhosis of the liver, lymphomatous diseases, rheumatoid arthritis, and myasthenia gravis excreted 11 to 100%, and patients with pernicious anaemia excreted 48 to 100%. There was no apparent relation between the presence or absence of free acid in the gastric juice in the miscellaneous group and the amount of $^{60}Co$ excreted. The administration of 100 ml. of neutralized normal gastric juice together with the vitamin $B_{12}$ to patients with pernicious anaemia reduced $^{60}Co$ excretion to 24 to 43%, whereas the addition of 2 mg. of folic acid and 25 mg. of an extract of hog's duodenal mucosa in 6 other cases of pernicious anaemia had no effect on $^{60}Co$ excretion.

The authors found, however, that on successive occasions there might be a two- to three-fold change in the " utilization " of the vitamin as measured in this way, and they suggest that such inconsistencies in their results, which differ from those of some other workers, may be due to the fact that they used a dose of 1·0 $\mu$g. of vitamin $B_{12}$ rather than 0·5 $\mu$g.

[It is clear from the numerous reports of experimental work with radioactive vitamin $B_{12}$ that it is important to standardize all technical procedures if comparable results are to be obtained.] *Janet Vaughan*

1663. **Estimation of Intrinsic Factor of Castle by Use of Radioactive Vitamin $B_{12}$**
S. T. CALLENDER, A. TURNBULL, and G. WAKISAKA. *British Medical Journal* [*Brit. med. J.*] **1**, 10–13, Jan. 2, 1954. 4 figs., 7 refs.

At the Radcliffe Infirmary, Oxford, the authors have estimated the absorption of vitamin $B_{12}$ (cyanocobalamin) by 10 normal subjects and by 13 patients with pernicious anaemia by measuring the radioactivity of the faeces after giving a test dose of vitamin $B_{12}$ labelled with radioactive cobalt ($^{60}Co$). A preparation of high specific activity (420 $\mu$c. per mg.) was used, a standard dose of 0·5 $\mu$g., containing approximately 0·2 $\mu$c., being given by mouth in 100 ml. of water. Food was then withheld for 2 hours and all stools collected in glass containers until a specimen was obtained containing less than 1% of the radioactivity of the test dose. A uniform homogeneous suspension of each faecal specimen was made in water, and the radioactivity of an aliquot portion estimated with a scintillation counter. The average count obtained over a period of 5 minutes from 50 g. of each of the faecal suspensions was compared with that from 50 ml. of a standard solution containing one-tenth of the test dose, and the faecal radioactivity expressed as a percentage of the total dose administered.

In the 10 normal subjects the total radioactivity recovered in the faeces was 20 to 40% of that of the test dose; this proportion was increased in the presence of infection. From the 13 patients with pernicious anaemia 76 to 101% of the radioactivity administered was recovered, but this figure was greatly reduced when a source of intrinsic factor, such as 100 ml. of pooled, neutralized, normal human gastric juice, a watery extract of gastric mucosa, or 10 mg. of the ammonium-sulphate-precipitated fraction of hog stomach mucosa, was given with the vitamin $B_{12}$. *Ernest T. Ruston*

## NEOPLASTIC DISEASES

1664. **A Contribution to the Pathogenesis of Acute Leukaemia.** (Beiträge zur Pathogenese der akuten Leukämie)
E. F. HUTH. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **74**, 1–19, 1953. 13 figs., bibliography.

Although the clinical picture and course of acute leukaemia in children are well known, it is only recently that important advances have been made in the study of the aetiology and pathogenesis, and hence in the treatment, of this condition. In this paper from the Medical Academy, Düsseldorf, the author briefly reviews the evidence indicating that leukaemia is a malignant disease, and reports the results of an investigation in which leukaemic blood was studied by phase-contrast and electron microscopy of Giemsa-stained preparations on polyvinyl films, and its metabolism also studied.

Maturation differences between leukaemic and normal blood cells are described, the most outstanding being an increase in size of the nucleus and nucleoli in diseased blood as the cells age, with ultimate disintegration of the nucleus. With the electron microscope a granular structure was observed in the nucleoli of leukaemic blood cells which formed a pattern different from that seen in normal and embryonic blood. Metabolic studies were found difficult, but differences in glycolysis in leukaemic cells were recognized and are attributed to deficiency of cytochrome-C. All the changes described are similar to those observed in the cells of carcinomatous growths in man and of tumours and leukaemic states in mice, and are regarded by the author as conclusive proof of a malignant factor in leukaemia. *Mary D. Smith*

1665. **A Contribution to the Treatment of Acute Leukaemia.** (Beiträge zur Therapie der akuten Leukämie)
E. F. HUTH. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **74**, 20–29, 1953. 3 figs., 44 refs.

Further to his study of the pathogenesis of leukaemia [see Abstract 1664], the author points out that a virus-like infection is known to be responsible for the production of several malignant tumours in vertebrate animals. While he believes that leukaemia in man is a malignant disease, he postulates that a virus-like factor may nevertheless be present in the leukaemic cells. He suggests that if this factor were accessible to chemotherapeutic action a non-specific interference with cell growth and consequent limitation of the leukaemic process might be brought about.

On this hypothesis he has treated, at the Children's Clinic of the Medical Academy, Düsseldorf, 5 cases of acute leukaemia with aureomycin, and in this paper he presents the results obtained, with clinical notes of 2 of the cases. Temporary remission in clinical signs was observed in all the patients, but only partial improvement in the haematological picture, and in all instances ultimate complete resistance to the antibiotic developed. He considers, however, that further investigation of selected cases in regard to the mode of action of aureomycin in the treatment of leukaemia would be worth while. The possible advantages of alternating this treatment with that with ACTH, cortisone, and aminopterin are discussed. *Mary D. Smith*

1666. **Lymphocytic Leukemia: an Analysis of Frequency, Distribution and Mortality at the University of California Hospital, 1913–1947**
M. B. SHIMKIN, E. L. LUCIA, K. C. OPPERMANN, and S. R. METTIER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 1254–1266, Dec., 1953. 5 figs., 22 refs.

Statistics are presented regarding the age at onset, sex, duration of illness and mortality of 149 patients with acute lymphocytic leukemia and 137 patients with chronic lymphocytic leukemia seen at the University of California Hospital, 1913 to 1947, inclusive. The data are compared with eight similar reports in the literature on acute leukemia and eight similar reports on chronic leukemia.

The age and sex distribution and duration of illness in acute lymphocytic leukemia have remained fairly constant during the period of study. There may have been a shift toward a higher age at onset among patients with chronic lymphocytic leukemia, but the sex distribution and duration of illness have remained fairly constant.

The mean duration of illness from onset to death in 149 cases of acute lymphocytic leukemia was found to

be 5·4 months. The duration of illness was longer among the age group 5 to 14 years than in age groups 0 to 4 years and 14 years and over, and was longer in patients with initially low leukocyte counts than in patients with high leukocyte counts.

The mean duration of illness from onset to death in 137 cases of chronic lymphocytic leukemia was found to be 42 months. No differences were present relative to age at onset or the initial leukocyte count.—[Authors' summary.]

1667. **The Prognosis of Treated Hodgkin's Disease. (Statistical Study of 182 Cases).** (L'avenir de la maladie de Hodgkin traitée. (Étude statistique d'après 182 cas)) A. DEVOIS and R. DECKER. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **30**, 197–203, Jan. 14, 1954. 5 figs., 5 refs.

The authors have analysed 182 cases of Hodgkin's disease (89 proved by biopsy) treated by radiotherapy at the Hôpital Tenon, Paris. The mean survival was about 3 years from the appearance of the first symptoms and 2¼ years from the first treatment, which accords well with the results in most other published series. In 21% of cases the patient survived 5 years or more, the longest individual survival period being 12 years. On the whole, women survived rather longer than men. The main clinical and haematological features are briefly analysed; enlargement of cervical lymph nodes was by far the commonest presenting sign.

[The statistical methods used by the authors are rather curious. The mean survival figures obtained by the methods usually employed in Great Britain would be rather longer than those given above.]

*P. C. Reynell*

1668. **Involvement of the Liver in Hodgkin's Disease. Differences between the Two Sexes.** (Atteinte hépatique dans la maladie de Hodgkin. Différences dans les deux sexes)
J. S. ABBATUCCI and E. C. BEATTY. *Bulletin de l'Association française pour l'étude du cancer* [*Bull. Ass. franç. Cancer*] **40**, 371–382, 1953. 1 fig., 27 refs.

The frequency of involvement of the liver in Hodgkin's disease and the influence of sex on the development of this complication was investigated in 82 cases (50 in men and 32 in women), coming to necropsy at the Memorial Hospital, New York.

Clinically, the liver was palpable in 53% of cases, but in those in which the enlargement was less than 4 finger-breadths below the costal margin there was often only non-specific change, such as chronic venous congestion or fatty infiltration. Very large livers were due to specific infiltration. In 42 of the 44 cases in which the liver was infiltrated there was concomitant splenomegaly. Jaundice was present in 23 cases, the cause in 19 being Hodgkinian infiltration, usually intrahepatic. There was invasion of almost all the portal tracts, with considerable sclerosis of the granulomatous lesion. In active lesions (Hodgkin's sarcoma), massive infiltration, with or without necrosis of liver tissue, may cause jaundice; in a few of the authors' cases the hepatic necrosis appeared to be due to nitrogen mustard. The greater frequency of the disease in males was confirmed, as was its greater severity, the average duration before death in males being 18·5 months compared with 26·8 months in females.

Hepatic involvement was present in 31 of the 50 men (62%) and in 13 of the 32 women (40%). It is inferred that infiltration of the liver is an indication of greater malignancy, as its incidence is not related to the duration of the disease. The suggestion that ovarian secretion affords relative protection was supported to some extent by the finding of atrophic ovaries in 7 of the 13 women in which the liver was invaded, including 3 patients aged 26, 30, and 31 respectively. Among the 17 women with no hepatic infiltration, only one showed ovarian atrophy.

*A. Piney*

## BLOOD-GROUP SEROLOGY

1669. **The Effect of Storage of Red Cells in the Frozen State on Blood Group Antigens.** [In English]
M. GROVE-RASMUSSEN, R. S. SHAW, Z. SOBKY, and E. M. CASNA. *Vox Sanguinis* [*Vox Sang. (Amst.)*] **3**, 119–122, Dec., 1953. 7 refs.

In experiments carried out at the Massachusetts General Hospital, Boston, erythrocytes were stored at −16° to −18° C. in two different media—the glycerol–citrate solution of Chaplin and Mollison and the glycerol–lactate solution of Brown and Hardin—an equal volume of the medium being added in stages to the packed cells with continuous agitation. Cells from 4 different donors were stored in each medium, the mixture in each case being divided between 8 small test-tubes before being stored.

At intervals of 2 to 6 weeks over a period of 20 weeks a tube from each batch was thawed at 37° C. for 30 minutes and centrifuged at 750 r.p.m. for 3 minutes. As much of the medium as possible was then removed and replaced by an equal volume of 15% trisodium citrate solution. After mixing and recentrifuging, the trisodium citrate was removed and the cells washed three times in 1% saline. Finally a 2% suspension of the cells was made in either 0·85% saline or AB serum and tested against antibodies to D, C, E, c, e, M, N, P, $Le^a$, $Le^b$, $Lu^a$, K, and $Fy^a$, the results being compared with those obtained with fresh cells from the same donor. Cells 20 weeks old were also tested with anti-S, anti-s, anti-k, and anti-$Jk^a$. No difference in agglutinability could be shown between cells stored in either medium and normal fresh cells.

*John Murray*

1670. **Anti-A and Anti-B Immune Antibodies in Pregnancy. Clinical Data of 240 Families.** [In English]
J. REEPMAKER and J. J. VAN LOGHEM. *Vox Sanguinis* [*Vox Sang. (Amst.)*] **3**, 143–161, Dec., 1953. 3 figs., bibliography.

The results of an investigation into the incidence of haemolytic disease among the children of 240 women whose serum contained anti-A or anti-B immune antibodies are described in this paper from the Central

Laboratory of the Amsterdam Blood Transfusion Service.

In 78 of the families symptoms of haemolytic disease or neonatal jaundice had occurred, but in 118 families no such symptoms had been observed. Many irregularities were observed, and no close correlation between the presence of immune antibodies in the maternal serum and the occurrence of haemolytic disease in the children could be found The pathogenesis, diagnosis, and treatment of haemolytic disease due to iso-immunization to A or B are discussed, and it is pointed out that for exchange transfusion of babies high-titre Group-O blood should not be used.

An examination of sera from a large number of normal controls (soldiers, blood donors, and pregnant women) showed that the incidence of $\alpha$ haemolysins was higher than that of $\beta$ haemolysins, that $\alpha$ haemolysins were commoner in Group-O than in Group-B subjects and in women than in men, and that the incidence of both $\alpha$ and $\beta$ haemolysins was highest among the pregnant women tested.

[This paper contains a great many valuable individual observations which cannot be abstracted; those interested in the subject are therefore advised to consult the original.]

*John Murray*

1671. **Factors Affecting Maternal Rh Immunisation.** [In English]

H. R. NEVANLINNA. *Annales medicinae experimentalis et biologiae Fenniae* [*Ann. Med. exp. Biol. Fenn.*] **31,** Suppl. 2, 1–80, 1953. 2 figs., bibliography.

## BLOOD TRANSFUSION

1672. **Prophylaxis against Post-transfusion Virus Hepatitis.** (К вопросу о профилактике посттрансфузионного вирусного гепатита)

S. I. SHERMAN, S. I. DIAKONOVICH, I. A. YURIKAS, A. I. BLINOVA, A. V. ALEKSEEVA, and R. S. GERMANT. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **31**, 57–61, Dec., 1953.

Between 1946 and 1952, the authors studied the relation between transfusion and viral hepatitis in 130 patients who developed the disease in from 30 to 270 days after a blood transfusion. The blood used for these cases came from 680 donors, of whom 36 had previously suffered from infective hepatitis, though in 19 the illness had occurred 2 to 4 years previously. Careful analysis of the 130 cases showed that only in 17 could the disease be definitely linked with the transfusion. Of 205 other patients who had received blood from some of the 680 donors, 14 developed infective hepatitis, but of these donors only one had had hepatitis, and he had given blood to only 2 patients in the group; the remaining 12 cases showed no relationship between the transfusion and the onset of the disease. Thus out of 144 victims of infective hepatitis following transfusion, there were only 19 who could be proved to have contracted it from blood donors.

In a second series of observations made from 1948 to 1951 it was found that blood taken from donors more than one month after they had recovered from infective hepatitis did not transmit the disease to recipients. A total of 129,596 donors were tested for their blood bilirubin content; in only 71 cases was this level raised, and of all these donors only 50 gave a direct qualitative reaction. None of those with an indirect reaction were in the pre- or post-icteric stage, nor were they found to have been in contact with viral hepatitis. Of the 50 with a direct reaction, 19 were in the pre-icteric and 17 in the post-icteric stage, although some of these had a normal bilirubin content; in the remaining 14 donors, infective hepatitis was not confirmed. The 36 with hepatitis were therefore excluded from the list of donors, and with this simple precaution the occurrence of transfusion hepatitis was prevented.

In the year 1952 a total of 43,809 donors were investigated, of whom 126 showed a raised serum bilirubin content, a direct reaction being obtained in 8 and an indirect reaction in 118. All those with raised bilirubin values and an indirect reaction were temporarily excluded from the list of donors until normal values from repeated bilirubin estimations and careful clinical observation showed that they were not suffering from viral hepatitis. The 8 donors who gave a direct reaction were all found, on further investigation in hospital, to have viral hepatitis. To elucidate the problem further, specimens of serum were taken from 6 donors, 4 of whom had given an indirect reaction and 2 a direct reaction. In the former the blood bilirubin content had been raised for 6 to 10 months, but in the latter 2 cases the bilirubin level had been increased for not more than 10 days. Complement-fixation reactions against the sera of known convalescents from viral hepatitis were negative in the first 4, and positive in the 2 with a direct reaction; the same results were obtained against sera from rabbits immunized against viral hepatitis.

The authors conclude that the direct (qualitative) reaction is a more reliable test for use in selecting donors, and that it could also be used in the prophylaxis of post-transfusion hepatitis. Donors found to have a raised serum bilirubin level and to give an indirect reaction should be placed under observation and only temporarily suspended from giving blood, as they are less likely to have early or recent hepatitis than those giving a direct reaction.

[The conclusion that patients who have had viral hepatitis are safe donors after one month's convalescence is surely rather a dangerous assumption, and does not support Tareev's statement that there are subacute and chronic forms of the disease. In the abstracter's view the safest procedure would be to exclude donors showing a raised serum bilirubin content until all tests are negative; this would of course also exclude all cases of persistent obstructive jaundice from any cause, but that would in any case be desirable.]

*L. Firman-Edwards*

1673. **Multiple Antibody Response to Repeated Transfusion: Development of a Hemolytic Isoimmune Antibody**

R. L. WALFORD, E. T. PETERSON, and T. NISHIHARA. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43,** 93–97, Jan., 1954. 5 refs.

# Respiratory System

1674. **The Syndrome of Cough Syncope**
A. KERR and V. J. DERBES. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 1240–1253, Dec., 1953. 4 figs., bibliography.

Cough syncope tends to occur mainly in heavily-built, obese males of middle age, especially in heavy smokers and drinkers. The authors state that many patients are unaware of the temporary loss of consciousness and that this fact may account for the apparently low incidence of the syndrome. Studies carried out in 40 cases showed that pressure in the pleural space, right atrium, right ventricle, superior vena cava, and femoral artery fell during an attack, but that the arterio-venous gradient was maintained. The authors therefore conclude that cough syncope is not due to any diminution of cerebral blood flow.

[It has recently been reported by Sharpey-Schafer (*Brit. med. J.*, 1953, **2**, 860; *Abstracts of World Medicine*, 1954, **15**, 237) that the central venous pressure may rise above the systemic arterial pressure during violent coughing, thus greatly reducing cerebral blood flow.]

*D. Weitzman*

1675. **Tic of the Respiratory Muscles. Report of Three Cases and Review of Literature**
W. DRESSLER and M. KLEINFELD. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 61–72, Jan., 1954. 2 figs., 26 refs.

## LUNGS AND BRONCHI

1676. **Etiology of Interstitial Plasma Cell Pneumonia.** [In English]
A. YLINEN, E. K. AHVENAINEN, and K. PENTTINEN. *Annales medicinae experimentalis et biologiae Fenniae* [*Ann. Med. exp. Biol. Fenn.*] **31**, 263–266, 1953. 5 refs.

An attempt was made at the Children's Clinic, University of Helsinki, to isolate a non-bacterial agent from patients with interstitial plasma-cell pneumonia, throat-swab preparations and specimens of blood from new untreated cases and lung tissue obtained at necropsy being used for a series of passage experiments in fertile hen's eggs, white mice, guinea-pigs, and kittens. After inoculation of the yolk sac or amniotic cavity of the hen's egg, the number of chick-embryo deaths was determined, yolk-sac preparations stained by Macchiavello's method were examined, and haemagglutination tests were performed on amniotic fluid. Under ether narcosis the animals were inoculated intranasally or intraperitoneally with amniotic fluid or lung or throat-swab preparations; in some instances specimens of blood were injected intramuscularly and subcutaneously. In all cases the lungs were examined histologically. One guinea-pig and one group of mice were given cortisone, but this failed to make the animals more susceptible to a possible virus infection. Bacterial complications in the animal experiments were controlled by injections of penicillin and streptomycin.

The results of these prolonged experiments were negative, except for a mild interstitial pneumonia in three kittens in which passages with a fresh lung preparation were made.

*D. Geraint James*

1677. **Deoxyribonuclease in the Treatment of Purulent Bronchitis**
P. C. ELMES and J. C. WHITE. *Thorax* [*Thorax*] **8**, 295–300, Dec., 1953. 5 figs., 11 refs.

Armstrong and White having shown (*Lancet*, 1950, **2**, 739; *Abstracts of World Medicine*, 1951, **9**, 579) that deoxyribonuclease reduced the viscidity of bronchial and pleural exudates both *in vitro* and *in vivo*, the present authors have carried out a controlled experiment at Hammersmith Hospital (Postgraduate Medical School of London) on a small group of patients with chronic bronchitis, in order to determine whether this finding is of any practical value. The deoxyribonuclease, obtained from pure beef pancrease, was given as an inhalation, 2·5 mg. being dissolved in a solution of 0·25% gelatin in M/100 magnesium chloride.

The enzyme reduced the viscidity of purulent sputum, but had no effect on mucoid sputum. Clinically, the results were disappointing, but the authors consider that this may have been because their dosage was inadequate. The production of mucus, its protective value in the respiratory tract, and the problems created by excessive mucus secretion are discussed. Although no definite conclusions could be drawn from the findings in this limited experiment, further investigation of mucolytic enzymes is urged, since, in the authors' view, the results of the present study suggest that these enzymes may be of value in the treatment of chronic respiratory infection, in conjunction with administration of suitable antibiotics.

*R. H. J. Fanthorpe*

1678. **Intrapulmonary Rupture of Hydatid Cysts of the Liver**
H. TOOLE, J. PROPATORIDIS, and N. PANGALOS. *Thorax* [*Thorax*] **8**, 274–281, Dec., 1953. 5 figs., 21 refs.

The clinical features of a severe, though rare, pulmonary complication due to rupture of a hydatid cyst of the liver are described in this paper from the Second Surgical University Clinic, Athens. If the expanding liver cyst is not operated on, rupture of the adventitia is inevitable. In most cases the cyst ruptures into the peritoneal cavity; less often it ruptures into the biliary passages. Cysts situated near the upper surface of the liver tend to grow upwards, elevating the diaphragm and

eventually rupturing into the pleural cavity or the bronchial tree; such a rupture is usually the sequel to suppuration in the cyst. This sequence is, however, uncommon, only 1 to 2·5% of all hydatid cysts of the liver behaving in this way. The commonest site for rupture is through the right dome of the diaphragm into the right lower pulmonary lobe. The cyst usually communicates with the lung through a relatively small aperture in the diaphragm which in turn either opens into a pulmonary cavity or communicates with the bronchus through a narrow sinuous track. In addition there may be a subphrenic abscess or an empyema, or both. In about 20% of cases the cyst also ruptures into the biliary tract.

Rupture is sudden in a little over half the cases; in the remainder the sputum gradually becomes purulent, bilious, and often foetid. A bile-stained sputum and expectoration of hydatid membrane are diagnostic of the condition. A positive reaction to intradermal and complement-fixation tests and an eosinophilia are valuable in diagnosis, but unfortunately the results of these investigations are frequently negative. In some cases the diagnosis can be confirmed by radiological examination. The lung shows an area of consolidation or a cavity, often associated with pleural involvement. The diaphragm is high. A gas-containing or calcified liver cyst is sometimes seen, but more often the cyst has collapsed and is thus invisible. Considerable help is obtained by injecting radio-opaque material into the pulmonary or the hepatic cavity, but these cavities are not always easy to locate.

The prospects of natural cure in these cases are poor, and the mortality with conservative treatment is 50%. Surgery, if it is to be successful, must be carried out before there are irreversible changes in the liver and the lung. The primary procedure in treatment is drainage of the liver cyst, the drainage being maintained until all flow of bile has ceased. Changes in the lung can be assessed at a later stage and lobectomy performed if necessary.

The authors describe 11 cases seen over a period of more than 20 years; there were 3 deaths—one immediately after drainage, one after a second operation for removal of hydatid membrane from the common bile duct, and one from haemoptysis 2 months after operation. [Little information is given about the state of the involved lung in these patients.] *W. P. Cleland*

1679. **Chronic Bronchitis. Factors in Pathogenesis and Their Clinical Application**
N. C. Oswald. *Lancet* [*Lancet*] **1,** 271–274, Feb. 6, 1954. Bibliography.

1680. **Benign Tumours of the Lung**
C. Price Thomas. *Lancet* [*Lancet*] **1,** 1–7, Jan. 2, 1954. 19 figs., 3 refs.

Benign tumours account for only about 2% of all tumours of the lung and bronchi. Of the 57 such cases here reviewed, 41 were cases of adenoma, 10 of hamartoma, 2 of endobronchial fibroma, and 4 were vascular tumours.

Although bronchial adenomata are believed by some American workers to be malignant and to arise from foetal rests, their histological resemblance to mixed salivary tumours and the fact that they may be endo- or extrabronchial lend strong support to the view that they are tumours arising from bronchial glands. The author believes adenomata to be benign because he has found that adequate conservative resection is hardly ever followed by recurrence, and malignant change was seen in only one of his 41 cases. The tumour is commoner in women, and tends to occur in the lower lobes, with or without extrabronchial extension. Histologically, the tumour is composed of cuboidal or spheroidal cells, regular in size and in staining properties. Rarely there is an excess of mucus. The lung distal to the tumour may be mildly or grossly bronchiectatic or may be almost unaffected, depending on the degree of obstruction and infection. The commonest symptoms are due to infection of the lung distal to the tumour, and include cough productive of purulent sputum and recurrent bouts of pneumonia, which occurred in 23 of the 41 cases. Haemoptysis from ulceration of the tumour appeared in half the cases. Non-productive cough, wheezing, dyspnoea, and " unilateral asthma " may be caused by the mechanical effects of the tumour, and it is stressed that the appearance of such symptoms should lead to further investigation by radiography and bronchoscopy in all cases.

The modern treatment is by resection, which should, however, be as conservative as possible. In early cases, a bronchotomy with local excision of the tumour is the treatment of choice. Excision of the tumour along with distal lung tissue should be performed when irreversible lung damage has occurred. The author emphasizes that many cases treated by pneumonectomy in the past would now be treated by local excision and bronchial repair. In one of 5 cases treated by local excision recurrence has necessitated pneumonectomy; in 31 other patients followed up from 4 to 14 years there has been no recurrence.

Hamartomata, the next most common type of tumour, are usually composed of cartilage with epithelial elements, but sometimes include fat, muscle, or connective tissue; they may occur in the lung parenchyma or as endobronchial tumours. They may present as symptomless " round foci " or with symptoms due to bronchial obstruction. The interstitial variety can usually be shelled out of the lung easily; the endobronchial type, unless extensive destruction in the distal lung has occurred, should be totally excised.

Vascular tumours are uncommon; they can be divided into arterio-venous fistulae and haemangiomata. Clinically, the classic features are polycythaemia, cyanosis, telangiectasis, and haemoptysis, but in some cases there may be no symptoms. All arterio-venous fistulae, and those angiomata that cause symptoms and are localized, should be excised. Fibromata are rare, and accounted for only 2 of the present 57 cases, both in women. They occurred as endobronchial tumours and the histological picture was of cellular fibromatous tissue covered by columnar epithelium, an appearance reminiscent of the fibro-adenoma of the breast. Both cases were treated

by resection of the tumour and the lobe of the lung beyond the obstruction.

Early recognition of these benign tumours can forestall the complicating element of infection, which induces a high morbidity, and permits of limited excision and thus of conservation of lung tissue. It is stressed that all patients who show an area of emphysema, or radiological evidence of over- or under-inflation of the lung, should be investigated by bronchoscopy, so that treatment may be carried out before irreversible damage has occurred. *A. M. Macarthur*

1681. **The Ventilatory Effects of the Head-down Position in Pulmonary Emphysema**

A. L. Barach and G. J. Beck. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 55–60, Jan., 1954. 2 figs., 20 refs.

At the Presbyterian Hospital, New York, the effect was observed of the supine, head-down position on pulmonary ventilation in patients with emphysema. Spirometry was carried out on 24 patients, each of whom was examined both sitting and tilted head down at the angle which appeared to give most relief of dyspnoea, and which in most cases was 16 degrees from the horizontal. With the patient breathing air, pulmonary ventilation in the head-down position was, on the average, 22% less than in the sitting position, whereas when 100% oxygen was substituted for air with the patient in the sitting position the average decrease in pulmonary ventilation was only 15%. Observations were also made on the oxygen and carbon dioxide content and the *p*H of arterial blood in 10 cases. In 6 of the 10 the arterial oxygen saturation was increased by tilting, while in all but 3 cases the carbon dioxide content and *p*H showed little or no change.

In the tilted patient clinical improvement in dyspnoea and decrease in pulmonary ventilation are due to an increased excursion of the diaphragm, elevation of which is helped by the pressure of the abdominal viscera. Similar results can be obtained by means of viscero-diaphragmatic breathing, abdominal belts, or pneumoperitoneum. *A. I. Suchett-Kaye*

## MEDIASTINUM

1682. **The Diagnosis of Primary Carcinoma of the Thymus.** (К распознаванию первичного рака зобной железы)

G. I. Vaĭnshteĭn and K. G. Nearonova. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **31**, 65–68, Dec., 1953. 1 fig., 5 refs.

A case of tumour of the thymus gland involving the heart and lungs is described in a woman aged 53, who when first seen complained of pain of a "squeezing" character in the cardiac region, radiating to the left arm, and of general weakness, nausea, and vomiting. She had suffered from hypertension for 6 years, and was asthenic and undernourished. Examination showed dilated veins over the 2nd and 3rd left intercostal spaces, diminished movement of the left side of the chest with weak breath-sounds, diminished vocal resonance, and dullness on percussion over the left base from the inferior angle of the left scapula downwards. The area of cardiac dullness was enlarged to 1 cm. outside the mid-clavicular line. The liver was palpated 3 cm. below the right costal margin, and the patient was very dyspnoeic. Electrocardiography showed lowered voltage, negative T waves in all three limb leads, and many other abnormalities. The temperature was slightly raised for 2 days, but later returned to normal. A diagnosis of coronary infarction was made.

In spite of treatment for cardiac failure, the dyspnoea and weakness continued. Pleural puncture was performed and 500 ml. of blood-stained fluid removed; it contained 1·8% of protein and a number of atypical cells. The patient's condition continued to deteriorate in spite of treatment with penicillin and streptomycin. Later on, radiography revealed a shadow in the anterior mediastinum, as well as collapse of the left main bronchus and displacement of the trachea to the right. Further electrocardiograms showed fresh myocardial infarcts, there was recurrence of pleural exudate in the left pleural cavity, and the patient died of cardiac failure 2 months after admission.

At necropsy a carcinoma of the thymus gland was found, extending into the pericardium, epicardium, and myocardium of all the heart cavities, with dissemination in the left pleural cavity and compression of the pulmonary veins and of the left main bronchus. The left lung was collapsed, and there were metastases the size of a pea around a vessel of medium calibre, numerous haemorrhagic infarcts in the lower lobes of both lungs, bilateral sero-fibrinous pleuritis, general atherosclerosis involving especially the aorta and left coronary artery, myocardial dystrophy, and "nutmeg" liver. Histological examination of the tumour showed a stroma of coarse spindle-celled connective tissue, along the columns of which were ranged atypical epithelial cells of round or oval form with weakly basophil protoplasm and vacuoles in many of the cells. The nuclei, which were of various sizes, stained deeply with haematoxylin, and Hassall's corpuscles were present. The periphery of the tumour consisted of a layer of fibrous connective tissue, with lymphoid cells diffused through it and forming small concentrations round the vessels. No metastases were found in the liver, spleen, adrenal or pituitary glands, bone marrow, or peripheral lymph nodes.

Some of the difficulties in the diagnosis of this case were due to the following facts: symptoms of mediastinal pressure were late in appearing; pleural effusion is not usually an early sign of thymic tumours but did occur early in this case; and the radiological evidence of mediastinal shadow and displacement of the trachea was not obtainable at an early stage owing to the patient's condition. Differential diagnosis from bronchogenic carcinoma depends chiefly on the occurrence in the latter of early and massive metastasis to the mediastinal lymph nodes, or of a spread of the primary growth from the bronchus to the mediastinum. Carcinoma of the thymus, unlike thymoma and lympho-epithelioma, is not readily detected by radiography.

*L. Firman-Edwards*

# Otorhinolaryngology

## EAR

1683. **Ménière's Disease. Successful Treatment by Minor Surgery**
S. ROSEN. *Lancet* [*Lancet*] **1**, 133–135, Jan. 16, 1954. 2 figs., 9 refs.

A method of treatment of Ménière's disease is described in which section of the chorda tympani nerve is performed under local analgesia. An incision is made through the skin of the lower half of the meatus 6 mm. external to the tympanic membrane, the skin being dissected up and the membrane elevated out of its sulcus. It may be necessary to tease out the nerve from the posterior wall of the middle ear. After section the membrano-cutaneous flap is replaced and rapid healing occurs. Of 50 cases so treated by the author at Mount Sinai Hospital, New York, complete cessation of the attacks of vertigo occurred in 27, a further 14 becoming free from major attacks.

The author found that experimental stimulation of the chorda tympani in these 50 cases produced vertigo alone in only one case, vertigo with tinnitus in 4 cases, tinnitus alone in 40 cases, and facial contraction in 48. Taste sensation was not elicited. The author suggests that the chorda tympani plays a part in the mechanism of Ménière's disease by virtue of the close proximity of the sensory ganglion of the facial nerve to the vestibular and cochlear nuclei in the medulla.

[The author's suggested explanation does not seem to offer any satisfactory theoretical basis for the procedure; the absence of vertigo on stimulating the nerve in all but 5 cases is noteworthy. Ménière's disease is subject to prolonged intermissions and fluctuations, and controlled observation in many cases is necessary before this procedure can be accepted as more than experimental.]

*T. A. Clarke*

1684. **Attachment of the Stapes to the Oval Window in Man**
H. BRUNNER. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **59**, 18–29, Jan., 1954. 10 figs., 26 refs.

The operation of mobilization or removal of the stapes for the relief of deafness or for Ménière's disease, originated by Kessel in 1876, was later abandoned because the results were uniformly disappointing and occasionally disastrous. Recently, with the development of chemotherapy and microsurgical technique, interest has revived in the operation of stapedectomy, which is difficult technically owing to the firm attachment of the stapes to the oval window. The present author suggests that the usual description of this attachment as by an annular ligament, relatively rich in elastic tissue, inserted on the frame of the oval window on the one hand and the footplate of the stapes on the other is too simple. The mechanical force acting on the foot-piece is mainly that of the stapedius on the anterior pole, which moves out towards the tympanic cavity eleven times as far from the window as the posterior pole moves in towards the vestibule. The bone of the window frame and the foot-piece, being brittle, enchondral bone, is liable to spontaneous fissure, so the ligament is inserted on cartilage in order to withstand this force. Frequently it joins the connective tissue of the fissula ante fenestram, which is also attached to a fold of mucosa extending between the crura and fastening the anterior crus of the stapes to the anterior wall at the niche of the window, thus further strengthening the stapedio-vestibular junction. For these reasons the operation might be easier if it were possible to incise the anterior portion of the annular ligament and so to mobilize the stapes by means of the unopposed contraction of the stapedius muscle.

*F. W. Watkyn-Thomas*

1685. **Some Aspects of the Sympathetic Nervous System in Relation to the Inner Ear.** [In English]
J. C. SEYMOUR and J. W. TAPPIN. *Acta oto-laryngologica* [*Acta oto-laryng. (Stockh.)*] **43**, 618–635, Dec., 1953. 10 figs., 15 refs.

In experiments carried out at the Ferens Institute of Otolaryngology, Middlesex Hospital, London, the authors have shown that stimulation of the cervical sympathetic trunk reduced the cochlear microphonic potentials for various sound intensities in 20 out of 23 cats. Post-mortem microscopical examination of the cochlea suggested that this phenomenon was caused by reduced secretion of endolymph of altered quality and that it was not due to the effect of lack of oxygen on the organ of Corti. It is suggested that a change in the sympathetic nerve supply to the ear may provoke some of the disorders of the inner ear, notably Ménière's disease.

*William McKenzie*

1686. **The Effect on the Hearing of Prolonged Stimulation of the Hearing Apparatus.** (Влияние на слух длительного применения слуховых аппаратов)
B. V. ELANTSEV and B. I. DUNAĬVITSER. *Вестник оториноларингологии* [*Vestn. Oto-rino-laring.*] 12–18, No. 5, Sept.–Oct., 1953. 4 figs.

In this investigation 97 tests were carried out on 50 patients, comprising 15 cases of nerve deafness, 18 of otosclerosis, 6 of chronic otitis media, 5 of adhesive otitis media, and 6 of mixed deafness. The tests were performed in a quiet room, and the stimulus was derived from records of speech and music, since these resemble the natural sounds to which the ear is exposed; only one test was made on the same patient in one day. The hearing was assessed audiometrically at frequencies of 128, 512, 2,048, 4,096, and 6,000 c.p.s, both by air and bone conduction.

After 1 to 2 hours of stimulation, slight changes were noted in the patients with nerve deafness, but these were

insufficient to be classed as fatigue. In patients with otosclerosis hearing sensitivity was lowered 5 decibels (db.) over the whole frequency range, but within 10 to 15 minutes after cessation of the stimulus the hearing sensitivity reverted to the pre-test level, suggesting adaptation or protective inhibition under the influence of adequately loud sound. The results in the cases of chronic otitis media and middle-ear adhesions were as indefinite as in those of nerve deafness. If stimulation was increased to periods of 5 to 8 hours, a rise in the threshold of 6 to 8 db. was noted in all the otosclerotic patients.

Observations were also made on the same patients before going to work and on return from work at the end of the day. These patients used hearing aids for 5 to 8 hours at their work, with a few breaks of 5 to 10 minutes each. Some improvement in hearing both by air and bone conduction was noted, but if the aid was used for an unbroken 8-hour stretch, lowered sensitivity to air conduction was found, though no worsening of hearing for the spoken voice was noted.

In a second series of investigations, 35 deaf patients, who had already used hearing aids for a year or more, were examined at intervals by audiometry over periods of 6 to 8 months, during which time the hearing aids were used regularly. In the majority of these patients hearing improved by 5 to 15 db. over the whole range irrespective of the type of deafness or type of hearing aid used, and many found that their speech discrimination had also improved. *Stephen Suggit*

## NOSE

1687. **Chronic Maxillary Sinusitis**
L. R. Boies. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 36–45, Jan., 1954. 3 figs., 5 refs.

The author considers that chronic maxillary sinusitis is curable by surgery. He describes the indications for operation and states his preference for intranasal antrostomy performed under local analgesia with a block of the second division of the fifth nerve. A hyperplastic condition involving other sinuses often indicates the presence of an allergic factor, and until this is controlled cure of the maxillary sinusitis is not possible. The incidence of chronic sinusitis seems to have been reduced in recent years by chemotherapy in the acute stage and by control of allergic factors.

*F. W. Watkyn-Thomas*

1688. **Management of Chronic Ethmoiditis and Sphenoiditis**
F. W. Dixon. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 46–47, Jan., 1954.

In the management of chronic ethmoiditis and sphenoiditis the author reserves surgery—apart from removal of polypi—for cases where the administration of antibiotics and the local application and instillation of ephedrine fail to improve the condition. Allergic factors should be dealt with, but if the allergen cannot be identified this is no bar to operation; in many cases allergic manifestations subside after operation. If the maxillary antrum is also infected, intranasal ethmoidectomy and sphenoidectomy are first performed; often the infection of the antrum will clear up once drainage and ventilation have been established, and further operation is unnecessary. *F. W. Watkyn-Thomas*

1689. **Management of Chronic Frontal Sinusitis**
L. F. Morrison. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 48–53, Jan., 1954. 8 refs.

Chronic frontal sinusitis, which the author defines as any case which has not cleared up after 30 days' treatment, is usually associated with ethmoid and maxillary sinusitis on the same side. Discussing local palliative measures, he condemns the use of adrenaline as likely to cause too intense an after-reaction; nor has he found the local application of antimicrobial agents satisfactory. If any chemotherapy is given it should be continued in high dosage for at least a week. Good results may be obtained from the administration of a shrinking agent such as ephedrine with barbiturates by mouth; as the agent is carried by the blood stream it reaches areas inaccessible to sprays, and its action, although slower in starting, is longer continued. The relief of pressure by trephining the external wall of the sinus may be the only local surgery needed; but it must be reinforced by resecting an obstructing septum, elimination of a concha bullosa, and elimination of infection in other sinuses. Attempts to establish permanent drainage by intranasal operations on the frontonasal duct usually fail, and the method has generally been discarded. The excellent results obtained by the intelligent use of antimicrobial agents in the relief of acute symptoms may produce a false sense of security; this is particularly true in respect of frontal osteomyelitis. "It is a well recognized fact that the antimicrobials are no substitute for surgical drainage of retained pus. The frontal sinus and its complications are no exception to this rule."

*F. W. Watkyn-Thomas*

1690. **Trauma to the Frontal Sinuses. Initial and Subsequent Care**
W. P. Work. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 54–64, Jan., 1954. 13 figs., 1 ref.

The author describes 12 cases of trauma to the frontal sinuses seen since 1949 and discusses the management of such cases. The most important part of initial treatment is to estimate the extent of injury to vital structures, such as the dura, whose exposure and repair, where necessary, are essential. Debridement should include removal of all loose bone and, where the patient's condition permits, ablation of frontal sinus and exenteration of ethmoid, when needed, is the method of choice, all traces of mucous membrane being removed to prevent cyst formation. When the frontal sinus is not ablated, patency of the frontonasal duct is maintained by means of an acrylic dilator which is worn for 6 months; in 10 of the 12 cases described, however, ablation of the frontal sinus was necessary.

[The most interesting point in the four papers abstracted above and in the discussion which followed

their presentation is the evidence of increasing conservatism in dealing with sinus infections in the United States—a trend noted also in Great Britain. The repeated warnings against blind trust in chemotherapy and the recognition of the importance of allergic factors are notable, as also is the fact that none of the authors appears to use antibiotics locally.] *F. W. Watkyn-Thomas*

1691. **Malignant Neoplasms of the Paranasal Sinuses**
L. R. CRANMER. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **58**, 704–709, Dec., 1953. 30 refs.

A review is presented of 89 cases of cancer of the sinuses treated at the University of Michigan Hospital, Ann Arbor, between 1932 and 1948. More recent cases are not included, nor are cases of skin neoplasm in which the sinuses were involved secondarily. There were 78 patients (average age 57) with some form of carcinoma, including a basal-cell growth without any external lesion of the skin, and 11 cases of sarcoma, in which the patients' ages ranged from 1 to 81 years.

In all cases the condition was advanced when first seen. The first sign noticed was swelling of the cheek or nose, around the eye, or of the forehead in 24, pain in 23, unilateral nasal obstruction in 14, oral symptoms in 10, nasal discharge in 8, frank epistaxis in 4, unilateral lacrimation in 2, and diplopia, proptosis, facial paralysis, earache, deafness, and numbness of the cheek in 1 case each. It is significant that the commonest presenting signs were those that could only be due to extensive growth, whereas early diagnosis is essential for successful treatment. It is made by careful examination, radiography with iodized oil, exfoliative cytology, exploration, and biopsy. Irradiation before surgery may lessen vascularity and diminish the size of the mass; but the best results are obtained with excision by electro-surgery or the actual cautery followed by irradiation, postoperative deformities being dealt with adequately by plastic surgery. The survival rate in the author's series was 22% at 3 years and 14% at 5 years. Results should be much better with earlier recognition, as metastases are rare (less than 8%) even in advanced cases. *F. W. Watkyn-Thomas*

## LARYNX

1692. **The Act of Deglutition after Total Laryngectomy.** (L'atto di deglutizione nei laringectomizzati totali)
P. BIONDETTI. *Radiologia medica* [*Radiol. med.* (*Torino*)] **39**, 1049–1083, Nov., 1953. 40 figs., bibliography.

After a comprehensive discourse on the anatomy, physiology, and mechanics of deglutition, the author describes a kymographic study carried out at the Institute of Radiology, Venice, of the swallowing of water and barium; a grid of 12 mm. was used and vertical and horizontal exposures were made. First a normal man was studied and the results then compared with those in 28 patients who had undergone total laryngectomy; 16 of the patients were examined twice, in 1947 and 1952, and 12 patients once only.

The variations in deglutition after laryngectomy are due to cicatricial changes in the anterior wall of the pharynx, the damage done to the muscles in this region, and interference with sensation, and are related to the degree of mutilation. If the neuromuscular apparatus has not been damaged, the reflex movements and the bulbar coordination remain normal. The voluntary movement of food from the tip to the base of the tongue and the reflex movements from there onwards are sometimes normal, but may be delayed; the lifting of the soft palate remains normal. Further transport of the bolus into the oesophagus is normally brought about by an aspirating and pumping action. After laryngectomy there is a preponderance of the aspirating action, and closure of the hypopharynx is incomplete, owing to abnormal movement of the posterior wall of the pharynx, which in the normal subject is immobile.

The sphincter at the entrance to the oesophagus remains normal in most patients. The trachea retains normal movement, but is slightly displaced towards the spinal column at the moment of the opening of the oesophagus. The reflex time in all the patients was about one-third to one-half longer than in the normal subject, and the act of swallowing was sometimes difficult, being performed with the help of movements of the mandible and head. Repeated examination showed that the function of the pharynx was stabilized in the first few months after operation, little further change in function being found at the second examination 5 years later. In patients who developed good pharyngeal speech after operation the residual pharynx was larger than in those who did not.

[Radiologists will find it useful to examine the many illustrations and technical details in the original paper.] *C. Eisinger*

1693. **Choice of Operation in Carcinoma of the Larynx**
A. J. CRACOVANER. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **58**, 655–664, Dec., 1953. 2 figs., bibliography.

In deciding the treatment to be adopted in a case of carcinoma of the larynx the important points to be determined are the extent of the growth—not its point of origin—for it is this that determines the route of spread, and the histological grade. A growth classified as Grade I or II is a well-differentiated, slow-growing tumour which does not spread early to the lymphatics; tumours of Grades III and IV are less differentiated, highly malignant, and spread rapidly through the lymphatics. The central necrotic area is not a reliable site for biopsy. Two possibilities must be remembered—infection and irritation may make a tumour look larger than it really is, but on the other hand submucosal spread may extend beyond the area visualized. The author holds that tomography should be used far more frequently in determining the outlines of a growth.

On the whole he accepts the generally recognized indications for the various types of operation, but he speaks well of hemilaryngectomy in cordal cases extending to the arytenoid, a procedure which has recently been successfully revived by several American surgeons. He strongly supports surgery as against irradiation as the treatment of choice. *F. W. Watkyn-Thomas*

# Urogenital System

1694. **Peritoneal Irrigation with Hydrophilic Colloids (Dextran) in the Treatment of Uraemia by Osmotic Principles.** (Peritonealspülung mit hydrophilen Kolloiden (Dextran) als osmotherapeutisches Prinzip bei der Urämie)

R. SCHUBERT, H. WERNER, and K. GENTERS. *Zeitschrift für die gesamte experimentelle Medizin* [*Z. ges. exp. Med.*] **122**, 208–234, 1953. 11 figs., 18 refs.

Experiments are reported from the University of Tübingen in which the therapeutic effect of peritoneal lavage with solutions of various hydrophilic colloids on uraemia was studied in rabbits. Colloids of molecular weights ranging from 15,000 to 80,000 were used, dissolved in saline, Tyrode solution, or water, with or without added dextrose, and the rabbits were made uraemic by the intravenous administration of mersalyl in doses of 22 mg. per kg. body weight. Lavage through a two-way catheter was started 2 days after the injection and was continued for 8 to 29 hours, a constant check being kept on the fluid balance, the blood urea and creatinine levels, and the amounts of these substances returned with the lavage.

The most satisfactory results were obtained with 10% " macrodex " in Tyrode solution without added dextrose, the molecular weight of this particular brand of dextran being believed to be between 62,000 and 80,000. Increasing the concentration to 20% did not improve the results. During an 8-hour experiment 504 mg. of urea was recovered from the lavage fluid, the blood urea level oscillating between 228 and 247 mg. per 100 ml. The serum creatinine level, however, rose from 3·2 mg. per 100 ml. at the beginning to 5·9 mg. per 100 ml. towards the end of the experiment. A total of 78·8 g. of the colloid was infused, but only 71·1 g. was found in the returned fluid; of the 7·7 g. lost, 0·8 g. could be traced in the circulating blood. The amount of colloid entering the circulating blood was considerably higher when dextrans of lower molecular weight were used, although these colloids are more soluble in water or Tyrode solution than those of high molecular weight.

*L. H. Worth*

1695. **The Nephrotic Syndrome**

J. R. SQUIRE. *British Medical Journal* [*Brit. med. J.*] 2, 1389–1399, Dec. 26, 1953. 11 figs., 10 refs.

The term " nephrotic syndrome " is reserved for patients with oedema, proteinuria, and hypo-albuminaemia, but without hypertension, haematuria, urea retention, or disturbance of electrolyte balance. It may occur in the course of glomerulonephritis or be associated with other diseases. The author, working with a number of colleagues at Birmingham University and using an osmometer of their own design, has shown that nephrotic plasma has a low colloid osmotic pressure and that its dilution with Ringer's solution gives proportionately smaller reduction of colloid osmotic pressure than in the case of normal plasma. The interstitial space is normally occupied by a gel whose " swelling pressure " plays a part in homeostasis, along with capillary hydrostatic pressure and plasma colloid osmotic pressure; in the nephrotic syndrome water has been imbibed by the gel so that the " swelling pressure " of the latter has fallen to zero and free fluid is present in the interstitial space, as is shown by the presence of dependent oedema that pits on pressure. Despite the anaemia, there is a reduced plasma volume.

All these factors have to be taken into consideration in discussing the mechanism of formation of oedema. An increase in plasma volume and total circulating plasma albumin content is associated with diuresis, and precedes a rise in plasma albumin concentration. The degree of hypo-albuminaemia can be demonstrated by electrophoretic studies. As the plasma albumin level falls to 1·5 to 2 g. per 100 ml. there is a corresponding fall in the total plasma protein concentration; at lower plasma albumin levels, however, the total protein value usually remains at between 5 and 5·6 g. per 100 ml. because of a corresponding rise in the $\alpha_2$ and $\beta$ globulins and fibrinogen content. Electrophoretic and quantitative studies of the urine of nephrotic patients have shown the ratios of the protein fractions in urine and serum to be in the following descending order of magnitude: albumin, $\alpha_1$ globulin, $\beta$ and $\gamma$ globulin, $\alpha_2$ globulin. (In acute nephritis the urine:plasma ratios for these fractions are almost identical.) Evidence is adduced from the alteration that ensues in these ratios following infusion of albumin which favours the concept that proteinuria in the nephrotic syndrome is largely due to a glomerular defect. The depletion of body protein and muscle wasting may be very gross. The loss of protein is brought about by the proteinuria and sometimes by amino-aciduria, the latter resulting from defective tubular reabsorption. A high protein intake is strongly recommended in these cases, and the administration of cortisone may benefit the patient by increasing appetite and therefore protein intake. What is needed is a drug which would reduce the proteinuria without diminishing glomerular filtration of substances of smaller molecular weight.

*K. G. Lowe*

1696. **Carbomycin in the Treatment of Enterococcal Urinary Tract Infections**

H. M. TRAFTON and H. E. LIND. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 43–47, Jan., 1954. 9 refs.

1697. **Renal Reabsorption of Bicarbonate**

D. D. THOMPSON and M. J. BARRETT. *American Journal of Physiology* [*Amer. J. Physiol.*] **176**, 201–206, Feb., 1954. 4 figs., 9 refs.

# Endocrinology

## PITUITARY GLAND

1698. **The Action of Pituitary Somatotrophin in the Prevention of Infections Favoured by Overdosage of Cortisone.** (Sur l'action de la somatotrophine hypophysaire dans la prévention des infections favorisées par le surdosage en cortisone)
P. DUCOMMUM and S. DUCOMMUM. *Annales d'endocrinologie* [*Ann. Endocr.* (*Paris*)] **14**, 765–771, 1953. 1 fig., 7 refs.

In order to confirm the finding of Selye (*Canad. med. Ass. J.*, 1951, **64**, 489; *Abstracts of World Medicine*, 1951, **10**, 523) that pituitary somatotrophic hormone can counteract the development of lowered resistance to infection caused by overdosage with ACTH and cortisone, the authors, working at the Institute of Experimental Medicine and Surgery, University of Montreal, carried out four experiments on rats the results of which are here described.

In the first experiment it was shown that the development of bacterial infection and the mortality from such infection were clearly promoted by the administration of cortisone in doses of about 20 mg. daily, and that this effect of cortisone could be counteracted by the simultaneous administration of pituitary growth hormone. In the second it was shown that growth hormone had no effect on connective tissue, as measured by the rate of migration of subcutaneously injected haemoglobin. In the third it was established, mainly by observations of changes in body weight of the animals, that the protective effect of growth hormone was not part of its general anabolic properties. In the fourth experiment they showed that growth hormone was less able to prevent infection in adrenalectomized rats. Finally, it was established that testosterone propionate, deoxycortone acetate, and oestradiol did not possess the " anti-infection " properties of growth hormone.

*B. Nordin*

1699. **The Effects of Administration of Hydrocortisone and Somatotrophic Hormone.** (Sur les effets de l'administration de l'hydrocortisone et de l'hormone somatotrope)
A. HORAVA and H. SELYE. *Annales d'endocrinologie* [*Ann. Endocr.* (*Paris*)] **14**, 772–778, 1953. 1 fig., 5 refs.

In this study of the nephrosclerosing action of hydrocortisone, alone and in combination with pituitary somatotrophic hormone, carried out at the University of Montreal, 24 male rats were divided into 4 groups. The first group acted as controls, the second received 2·5 mg. of hydrocortisone subcutaneously daily, to the third pituitary growth hormone was given three times daily subcutaneously, and the fourth group received both substances. At the end of 3 weeks the animals were killed and examined.

It was confirmed that hydrocortisone produced severe loss of weight, atrophy of the adrenal and thymus glands and of the spleen, mild glomerular lesions, slight elevation of the blood pressure, and necrotic foci in the lungs. Growth hormone did not prevent the adrenal and thymic atrophy and it aggravated the renal lesions, but it did prevent the appearance of infected foci in the lungs and also the severe loss of weight. The possible mechanism of this action is discussed and several hypotheses are proposed.

*B. Nordin*

1700. **The Influence of Reichstein's Compound L on Certain Effects of the Administration of an Anterior Pituitary Extract.** (Influence du composé L (de Reichstein) sur certains effets de l'administration d'un extrait du lobe antérieur de l'hypophyse)
A. HORAVA, R. GUILLEMIN, and H. SELYE. *Annales d'endocrinologie* [*Ann. Endocr.* (*Paris*)] **14**, 779–783, 1953. 1 fig., 4 refs.

In this further study [see Abstract 1699] of the role of steroids in the pathogenesis of nephrosclerosis the effect of Reichstein's Compound L (allopregnane-3:17-diol-20-one) was investigated in experiments on young rats of both sexes which had undergone unilateral nephrectomy and had been rendered hypertensive. Reichstein's Compound L and anterior pituitary extract were administered to the first 2 groups, a third received both substances, and a fourth acted as controls. It was found that the hypertensive and diuretic effects of anterior pituitary extract were significantly inhibited by Compound L, but that there was little if any effect upon the histological picture of nephrosclerosis. Administration of both substances together caused hypertrophy of the mammary and preputial glands in both sexes.

*B. Nordin*

## THYROID GLAND

1701. **Theory of Thyroid Hormone Action. Conclusions Derived from Differences in Effect of Sodium L-Thyroxine, Sodium D-Thyroxine, Triiodothyronine, and Potassium Iodide on Uptake of Radioactive Iodine by Thyroid Gland of Normal Human Subjects**
P. STARR and R. LIEBHOLD-SCHUECK. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 880–888, Dec., 1953. 1 fig., 9 refs.

Working at the University of Southern California and Los Angeles County Hospital, the authors investigated the action on healthy volunteers of sodium L-thyroxine given in a daily dosage of 25 to 50 $\mu$g., triiodothyronine in a dosage of 4 to 140 $\mu$g., sodium D-thyroxine in a dosage of 100 to 500 $\mu$g., and potassium iodide in a dosage of 0·42 to 4·2 mg. over a period of one week. Radioactive iodine ($^{131}$I) was given in tracer doses before

and just after the course of medication, and counts were made over the thyroid 24 hours later, allowance being made in the second count for any residual $^{131}I$ in the gland. Measurements of the blood protein-bound iodine content were also made before and after the course of medication. It was shown that at least five times as much iodine must be given in inorganic form as in hormonal combination to depress the uptake of $^{131}I$ by the normal thyroid gland. Sodium D-thyroxine appeared to reduce the iodine uptake, but this may have been due to contamination with the laevo isomer.

Triiodothyronine produced its maximum effect on $^{131}I$ uptake in doses of 8 $\mu$g. a day, a larger dose being no more effective. It was more than five times more potent than thyroxine, and produced a fall in the serum protein-bound iodine level, which was increased by sodium L-thyroxine.

It is suggested that triiodothyronine is secreted at times of acute stress, the gland normally producing only thyroxine. Possibly triiodothyronine is produced in excess in Graves's disease, whereas a hyperfunctioning adenomatous goitre produces an excess of thyroxine. Testing for one or other of these substances in the urine in such cases is suggested as a further line of research.

*G. S. Crockett*

1702. **The Value of a Single Injection of Thyrotropin in the Diagnosis of Obscure Hypothyroidism**
W. M. JEFFERIES, R. P. LEVY, W. G. PALMER, J. P. STORAASLI, and L. W. KELLY. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 876–884, Nov. 26, 1953. 4 figs., 16 refs.

In this paper from Western Reserve University and Hospital, Cleveland, the authors describe a test designed to differentiate hypothyroidism of pituitary origin from that due to primary lack of thyroid function. It is based on the earlier observation of Astwood and Stanley (*Endocrinology*, 1949, **44**, 49; *Abstracts of World Medicine*, 1949, **6**, 454) that a single injection of thyroid stimulating hormone (T.S.H.) increased the rate of uptake of radioactive iodine ($^{131}I$) by the thyroid gland. The test is carried out as follows. At 9 a.m. a tracer dose of $^{131}I$ (10 $\mu$c.) without added carrier is given by mouth to the fasting subject. The activity of the thyroid gland is measured 3 hours later, and immediately afterwards an intramuscular injection of 10 mg. of T.S.H. is given. Then, 24 hours after the first dose of $^{131}I$, the residual activity of the thyroid is measured, and this is followed by a second tracer dose of the same radioactivity as the first; 3 hours later the activity of the thyroid is again estimated. The effect of the T.S.H. is evaluated by the difference in the results of the two determinations of thyroid gland activity.

In 2 normal subjects tested first as controls, 10 mg. of T.S.H. produced a rise of some 50% in the thyroid uptake of $^{131}I$, the increase occurring whether or not there had been previous medication with thyroid; this characteristic of the test is obviously a great clinical advantage. The effect did seem to be masked, however, by the previous ingestion of iodine, but the serum protein-bound iodine level still increased under these circumstances. Application of the test to patients with primary hypothyroidism showed that there was no increase in the uptake, but that in patients with hypopituitarism there was.

In a number of patients in whom initial iodine uptake was normal or near normal, uptake was not stimulated by administration of T.S.H. This was interpreted as indicating that these patients had little or no thyroid reserve.

The authors point out that the test described is simple to perform, takes little more time than an ordinary 24-hour uptake test, and should prove a useful tool in the diagnosis and study of thyroid dysfunction.

*G. A. Smart*

1703. **Pathology of Spontaneous Myxedema in the Aged**
P. A. BASTENIE. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **1**, 845–849, Dec., 1953. 1 fig., 14 refs.

It is pointed out that spontaneous myxoedema is mainly a disease of the aged caused, in most cases, by atrophy of the thyroid gland, the nature of the atrophy being still undetermined. During a recent 21-year period 29 cases of severe hypothyroidism were studied post mortem at the University of Brussels. In 22 patients (aged 58 to 84 years at the time of death) the cause of the myxoedema was primary thyroid atrophy, and in 7 (aged 50 to 72 years) the primary lesion was in the pituitary. Microscopical examination of the thyroid in the former group showed that the parenchyma was reduced to remnants of cells in heaps enclosed in dense inflammatory tissue, with marked degenerative changes. In 6 cases there were nodules of cells derived from the thyroglossal tract. The term " atrophic thyroidosis " is suggested for this group. In the 7 patients (all women) with secondary hypothyroidism there were severe destructive lesions in the pituitary, and marked colloid involution in the thyroid, with little inflammation or parenchymatous degeneration. In these cases, in contrast to those of primary hypothyroidism, splanchnomicria was present.

Examination of 100 thyroid glands from patients aged 20 to 80 years indicated that clinical myxoedema results from a slow destructive process. The author suggests that there is pituitary compensation for thyroid atrophy, which stimulates the activity of the thyroid but ends by causing its exhaustion.

*J. N. Agate*

1704. **Metastases of Benign Thyroid Adenoma in the Lung.** (О метастазах доброкачественной аденомы щитовидной железы в легкие)
S. A. LOMONOSOVA. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 55–57, Dec., 1953. 1 fig., 5 refs.

The commonest benign tumours of the lung are bronchial adenomata—although some authors hold that these are really tumours of low-grade malignancy—the next most common are chondromata, while cases of fibroma, fibromyoma, myoma, lipoma, papilloma, and haemangioma have been described in individual patients, but are much rarer.

In the case described in this article there were numerous tumours arising from a benign adenoma of the thyroid.

The patient, in whom the disease had existed for 15 years, was a woman aged 32. She had noticed a mass occupying the whole of the right side of the neck made up of lumps the size of a plum, and also two swellings on the left side, all of which had appeared at the age of 12, but had become considerably enlarged at the age of 17; on examination they resembled enlarged lymph nodes. Radiography of the chest revealed multiple shadows, most of which were of rounded form. At first she was regarded as a case of disseminated tuberculosis of haematogenous origin and also, in view of a persistent tachycardia, slight exophthalmos, and a raised metabolic rate, was believed to have Graves's disease. The temperature, however, was normal, her general condition good apart from dyspnoea, and signs and symptoms showed little change for 14 years. The radiographic appearances at the end of this time being unchanged and lymphogranulomatosis (Hodgkin's disease) having been excluded, the choice of diagnosis lay between cysticercosis and metastases from some benign tumour. Blood examination showed the haemoglobin value, cell count, and sedimentation rate to be normal. No radiological changes were discovered in the stomach, bowel, skull, or bones of the leg. There was marked enlargement of the veins on the left side of the neck and the external aspect of the left knee, however, and these veins were tender to touch. Biopsy of one of the tumours on the left side of the neck showed the structure and cellular elements of thyroid tissue. *L. Firman-Edwards*

## ADRENAL GLANDS

1705. **Prolonged Cortisone Therapy in the Congenital Adrenogenital Syndrome.** (Die Cortisondauerbehandlung des kongenitalen adrenogenitalen Syndroms)
A. PRADER. *Helvetica paediatrica acta* [*Helv. paediat. Acta*] **8**, 386–423, Nov., 1953. 14 figs., 46 refs.

The author reports the results of the treatment with cortisone of 10 female and 4 male patients with congenital adrenocortical hyperplasia. The ages of the females ranged from 3 to 30 years, and of the males from 6 to 36. Six of the former had undergone unilateral adrenalectomy without improvement, followed by oestradiol implantation in doses ranging from 40 to 280 mg.; 6 (4 of them under 14) had undergone amputation of the enlarged clitoris; and 3 had received a short course of cortisone some time previously.

All 14 patients were treated with cortisone for periods of 3 to 20 months (average 13 months). The drug was given by mouth in 3 doses totalling 25 to 75 mg. daily, intramuscularly in doses averaging 75 mg. every fourth day, or in the form of " depot-cortisone ", a long-acting suspension of cortisone crystals up to 100 $\mu$ in size, of which a single injection of 600 to 800 mg. was given monthly. The clinical effects were identical with all three methods of administration, and there were no side-effects in the 2 cases treated with depot-cortisone. The dosage was adjusted to that which kept the urinary excretion of 17-ketosteroids just below 8 mg. daily in the older patients, and which caused minimal inhibition of growth in the younger patients. Some of the patients were admitted to hospital for the first 2 or 3 weeks, but for the most part treatment was given at home, the patients sending urine for 17-ketosteroid estimation and attending as out-patients every 2 or 3 months. Sodium intake was not restricted and no extra potassium was given.

The treatment was uniformly successful, the main results being as follows: (1) acne disappeared within a few weeks; (2) within 1 to 3 months the older girls became more feminine in appearance and their breasts developed; (3) the testicles of the older boys began to mature and testicular tumours became smaller; (4) hirsuties regressed in the older girls and did not develop in the younger children; (5) there was a rise in pitch of the voice in the older girls; (6) marked pigmentation disappeared; (7) increased rate of growth and of skeletal development in the younger children was prevented; (8) the haemoglobin value, if increased, became normal; (9) the psychological effects of the glandular disturbance were improved; and (10) menarche occurred, usually within 7 months.

No untoward side-effects were seen, even after 20 months' treatment. When treatment was stopped, however, recurrence of symptoms was the rule. The author recommends that treatment be started early in childhood and continued for years, strict supervision in regard to 17-ketosteroid excretion, blood pressure, growth, and weight being essential. With older patients, the desirability of treatment must be decided on its merits in each case. *V. C. Medvei*

1706. **Ascorbic-acid Metabolism after Administration of Corticotrophin**
R. R. MCSWINEY, B. E. CLAYTON, and F. T. G. PRUNTY. *Lancet* [*Lancet*] **1**, 178–182, Jan. 23, 1954. 5 figs., 17 refs.

The disappearance of ascorbic acid from the adrenal cortex on injection of corticotrophin (ACTH) has been noted by a number of workers as occurring in a variety of animals. But whether the ascorbic acid is consumed within the cortex or extruded into the plasma has never been clearly demonstrated. At St. Thomas's Hospital, London, the present authors have investigated changes in the quantity of reduced ascorbic acid and its immediate oxidation products in the plasma and urine of patients treated with ACTH and in the urine of guinea-pigs given injections of the hormone.

The reduced ascorbic acid value was determined by titration with dichlorophenolindophenol; direct determination was made in the case of plasma, but for urine, which contains interfering substances, the " formaldehyde correction " procedure developed by Snow and Zilva (*Biochem. J.*, 1944, **38**, 458) was followed. The amounts of the immediate oxidation products of ascorbic acid, namely, dehydro-ascorbic acid and diketogulonic acid, were also determined, the former by reduction with hydrogen sulphide and the latter by the method of Roe and Kuether (*J. biol. Chem.*, 1943, **147**, 399).

Six patients receiving treatment with ACTH were studied. All were given a diet containing no more than

40 mg. of ascorbic acid per day, which was supplemented in 2 cases by 300 mg. per day and in one case by 30 mg. per day. After a stabilization period, and before administration of ACTH, 2 of the patients were found to have a high initial ascorbic acid level in the plasma (greater than 1 mg. per 100 ml.), 2 had an intermediate initial level (0·75 to 1·0 mg. per 100 ml.), and 2 a low initial level (less than 0·6 mg. per 100 ml.). The patients with high and intermediate initial levels responded similarly to administration of ACTH, showing increased output of ascorbic acid in the urine for the first 2 or 3 days only; the dehydro-ascorbic acid output was also increased in one case but not in the others; plasma determinations showed a tendency for the levels of oxidation products of ascorbic acid to rise at first and then fall with continued therapy. The findings in guinea-pigs with adequate intake of ascorbic acid were similar. Patients with low ascorbic acid saturation did not, however, show these changes.

The increase in output is probably due to three causes, namely, increased renal clearance of ascorbic acid, a passive shift of ascorbic acid from cells to extracellular fluid with the usual shift of water, and a further transfer of ascorbic acid in the same direction due to some unidentified mechanism. *Nancy Gough*

## DIABETES MELLITUS

1707. **Chemical Findings in Infants Born of Diabetic Mothers: a Preliminary Report**
B. D. Graham and G. H. Lowrey. *University of Michigan Medical Bulletin* [*Univ. Mich. med. Bull.*] **19,** 267–272, Oct., 1953. 13 refs.

Abnormal chemical changes in the blood of 11 newborn infants of diabetic mothers are described in this paper from the University of Michigan. A comparison with the findings in the normal infant showed that in the infant born of a diabetic mother the *p*H of the blood was lower and the plasma chloride and total base levels " varied extremely ". In this small series there appeared to be a direct correlation between the severity of the acidosis and the abnormal clinical findings, which included cyanosis, lethargy, inability to suck, and oedema. There was a high plasma carbon dioxide tension (capillary blood) indicating lack of control of respiration, either central or pulmonary. The authors stress that the high mortality in these children is not due to hypoglycaemia, because the blood sugar level is low in all infants in the first few days of life. *I. McLean-Baird*

1708. **Studies on Hypoglycemia Responsiveness**
S. S. Lazarus and B. W. Volk. *Metabolism* [*Metabolism*] **2,** 500–509, Nov., 1953. 1 fig., 46 refs.

This communication from the laboratories of the Jewish Sanitarium and Hospital for Chronic Diseases, Brooklyn, New York, describes experiments carried out on animals to elucidate the mechanism of " hypoglycaemia responsiveness ". The authors point out that after an intravenous injection of insulin the blood sugar content in normal subjects falls sharply for 20 to 30 minutes, after which it slowly returns to the initial level, which it reaches within 150 minutes. This recovery is not due to the cessation of action of insulin, the effect of which can be observed for much longer than 30 minutes in diabetics, but is due to some mechanism for restoration of the blood sugar level which operates in response to hypoglycaemia and which is deranged in pituitary or adrenal insufficiency.

In an attempt to establish the nature of this mechanism, insulin tolerance tests were performed on five groups of dogs: (1) 10 normal untreated controls; (2) 3 adrenalectomized controls and 5 adrenalectomized dogs which received 1 mg. of pituitary growth hormone per kg. body weight subcutaneously on each of the 2 days preceding the test; (3) 5 hypophysectomized dogs which were given 50 mg. of corticotrophin (ACTH) for the first 3 weeks after operation, the test being performed at the end of this time and repeated after a further 3 weeks without ACTH; (4) 3 dogs which had been subjected to adrenomedullectomy, 3 to total sympathectomy, and 2 to both procedures, together with 6 intact dogs, all 14 being given tetraethylammonium chloride, hexamethonium, or benzodioxane (piperoxan) at the time of the test; and (5) 5 pancreactomized dogs.

The pattern of hypoglycaemia responsiveness established in the normal animals was unchanged in the adrenalectomized animals which received growth hormone, in the hypophysectomized dogs after receiving ACTH for 3 weeks, and in all the animals in Groups 4 and 5. Only in the adrenalectomized animals not given growth hormone and in the hypophysectomized animals after ACTH had been omitted was there a lack of response to hypoglycaemia. The authors therefore conclude that the liver responds directly by glycogenolysis to the stimulus of hypoglycaemia and that the various endocrine factors affect hypoglycaemia responsiveness indirectly only, in that they determine the blood sugar level at which the response will occur, and maintain glycogen storage in the liver at an adequate level.
*I. McLean-Baird*

1709. **Pharmacologic and Clinical Studies on Two New Types of Long-acting Insulins with Special Reference to Zinc Insulin Preparations (Novo): a Preliminary Report**
J. L. Izzo. *Diabetes* [*Diabetes*] **2,** 358–364, Sept.–Oct., 1953. 6 figs., 8 refs.

In the study reported in this paper from the University of Rochester, New York, the properties and duration of action of a new experimental zinc insulin preparation (referred to as No. 2958) similar to the " novo " preparation, " ultra-lente " (insulin zinc suspension (crystalline)), were compared with those of a clear acid solution of chemically modified insulin (special insulin 190-4B-111) and with those of NPH insulin.

In comparing the solubility of the preparations in serum, it was shown that insulin 2958 dissolved at a definitely slower rate than NPH insulin, the latter being practically all in solution by the 5th hour, whereas less than 50% of insulin 2958 was dissolved at the end of 5 hours and only 75% at the end of 24 hours. The solubility of the new preparation was therefore similar

to that of standard protamine zinc insulin, except that the solubility curve was more uniform. (Comparative solubility properties of insulin 190-4B-111 could not be studied in the same way, as it is already in solution.) Comparison of daily patterns of insulin activity was based on the response of blood and urinary sugar levels to single doses of each type of insulin given on 4 to 7 consecutive days. Blood sugar levels were determined at 8.0 and 11.30 a.m. and 4.30 and 9.30 p.m. In unstable diabetics insulin 190-4B-111 consistently produced low blood sugar concentrations at 11.30 a.m. or 4.30 p.m. and high concentrations at 9.30 p.m. or 8.0 a.m., whereas insulin 2958 produced a low level at 8.0 a.m. and high levels at 4.30 p.m. and 9.30 p.m. The pattern of NPH was qualitatively similar to that of insulin 2958, but its activity was more nearly constant.

Clinically, no large differences in timing were noted with insulins NPH, 2958, and 190-4B-111 in stable diabetics, but the expected differences were observed in unstable cases. Postprandial glycosuria was less well controlled with insulin 2958 than with NPH, and attempts to correct this glycosuria by increasing the dose of insulin 2958 tended to cause nocturnal hypoglycaemia. Insulin 190-4B-111 tended to produce hypoglycaemia during the middle of the day.

From these results the authors conclude that the duration of action of insulin 190-4B-111, in common with that of other clear insulin preparations, is insufficient to span 24 hours adequately in unstable diabetics. Their findings in respect of insulin 2958 confirm the reports of Hallas-Møller *et al.* (*Ugeskr. Læg.*, 1951, **113**, 1761 and 1767) that a preparation at least as long-acting as protamine zinc insulin can be obtained by suspension of pure insulin and zinc alone, in proper concentrations in buffering media. They also consider that suitably timed zinc insulin preparations might have certain advantages over NPH insulin, such as more uniform absorption from the subcutaneous depot and fewer hypersensitivity reactions, and allow greater flexibility in the timing of injections. *J. Lister*

1710. **Nature and Prevention of Local Skin Lesions from Insulin Administration. Observations on 100 Patients**
M. Fabrykant and B. I. Ashe. *Metabolism* [*Metabolism*] **3**, 1–10, Jan., 1954. 1 fig., 18 refs.

At the Bellevue and University Hospitals, New York, the authors studied the incidence of skin lesions at the site of insulin injection in relation to the technique employed in 100 unselected diabetic patients from hospital and private practice. The patients were seen every 2 to 6 weeks over a 10-month period. It was found that diabetics gave themselves insulin in one of four ways: (*a*) by slanting injection into the pinch-folded skin (the conventional method); (*b*) by perpendicular injection into pinch-folded skin; (*c*) by an automatic syringe; and (*d*) by perpendicular injection into the stretched skin, the method recommended by the authors. There were three types of lesion: (1) local inflammatory reaction with itching, tenderness, redness, and swelling; (2) local painless induration; and (3) lipodystrophy, in the form of fat atrophy or fat hypertrophy. Lesions were considered to be "persistent" if they developed after each injection. Type-1 lesions, either alone or in combination with Type-2 and Type-3 lesions, were the most frequent. No relationship was found, however, between the incidence of lesions and the type of insulin used for the injection.

Of 72 patients using the conventional injection method 63 had skin lesions (persistent in 42). Lesions were observed in 4 of 10 patients using a perpendicular injection into pinch-folded skin and in 2 of 5 patients using an automatic syringe. Of the 13 patients following the recommended method of perpendicular injection into the stretched skin, 6 had skin lesions, but in none were the lesions persistent. In 42 patients who changed from the conventional to the recommended method there was a reduction in the incidence and severity of the local lesions. Of the 100 patients, 25 were consistently free from skin lesions. The authors conclude that these local skin lesions are due to mechanical and chemical action of injected insulin, and that the aetiology of insulin lipodystrophy is similar. Local metabolic action of insulin was not considered important.

[The conclusions drawn from this relatively small study are unlikely to be accepted by many interested in this subject. They are not in accord with the more elaborate studies of others, particularly those of Marble and Renold (*Trans. Ass. Amer. Phys.*, 1949, **62**, 219) and of Renold, Marble, and Fawcett (*Endocrinology*, 1950, **46**, 55).] *J. N. Harris-Jones*

1711. **Effect of Purified Glucagon (Hyperglycemic–Glycogenolytic Factor, HGF) on Carbohydrate and Corticoid Metabolism in Normal and Diabetic Subjects**
W. R. Kirtley, S. O. Waife, O. M. Helmer, and F. B. Peck. *Diabetes* [*Diabetes*] **2**, 345–349, Sept.–Oct., 1953. 6 figs., 12 refs.

Commercial insulin has long been known to contain a hyperglycaemic–glycogenolytic factor to which Kimball and Murlin (*J. biol. Chem.*, 1923, **58**, 337) gave the name glucagon. In order to determine its effects in man, the present authors administered a purified preparation of glucagon to normal subjects and to patients with diabetes of varying degrees of severity. (A unit of glucagon is defined as the amount per kg. body weight which on intravenous administration into a 24-hour-fasted, anaesthetized cat produces a rise in the blood sugar level of 30 mg. per 100 ml. within 25 minutes.) The dose used in these studies carried out at the Indianapolis General Hospital was 20 units per kg. body weight given intravenously over half an hour. All the subjects were fasted and the diabetic patients received no insulin on the morning of the test, in which determinations of the blood levels of glucose, pyruvate, lactate, inorganic phosphate, and potassium were made before and at intervals after the infusion of glucagon. Fractional determinations of the urinary 17-hydroxycorticoids and 17-ketosteroids, together with urinary creatinine excretion, were also made. Several subjects were also given an adrenaline tolerance test (0·01 ml. of a 1 in 1,000 solution of adrenaline per kg. body weight intramuscularly).

In the normal subjects, blood glucose levels were maximal at the end of the glucagon infusion, and fell to below initial levels after 60 to 90 minutes. The blood pyruvate level rose after administration of adrenaline but fell after infusion of glucagon. In stable, obese, middle-aged diabetics, blood glucose levels were abnormally elevated after both glucagon and adrenaline, while the blood pyruvate level rose after adrenaline but not after glucagon. On the other hand, in unstable, usually young, thin diabetics, the blood glucose level did not rise as high after glucagon as in the stabilized diabetic patients or normal subjects, while after injection of adrenaline, blood glucose and pyruvate values rose to unusually high levels and that of inorganic phosphate fell, indicating active phosphorus utilization. The ratio between 17-hydroxycorticoid excretion and creatinine excretion indicated that in both diabetic and normal subjects there was some stimulation of steroid excretion during the hour in which glucagon was given.

The authors suggest that the differences in response to glucagon in different types of diabetics are probably related to the amount of liver glycogen immediately available. They believe that the unstable diabetic is deficient in liver glycogen and hence shows only a small rise in blood sugar level after glucagon, whereas the stable diabetic has a larger glycogen store, allowing a greater glucagon response. They consider that the enhanced 17-hydroxycorticoid excretion during the hour of glucagon infusion may have been due to adrenal stimulation as a result of the non-specific stress resulting from the infusion, but note also the possibility that the rate of excretion of steroids by the kidney may be increased. *J. Lister*

1712. **Non-reducing Carbohydrate in the Blood Filtrate of Diabetics, as Indicated by Determination of the Residual Carbon.** (Über nicht reduzierende Kohlenhydrate im Blutfiltrat von Diabetikern, dargestellt auf Grund von Bestimmungen des Restkohlenstoffs)
P. H. SCHULITZ. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 1182–1185, Dec. 5, 1953. 3 figs., 15 refs.

At Barmbek General Hospital, Hamburg, the sugar and residual carbon content of 300 blood filtrate samples from diabetic and healthy subjects was determined by the author's own method (*Hoppe-Seyl. Z. physiol. Chem.*, 1951, **288**, 142). In the diabetic patients the residual carbon values were higher (150 to 220 mg. per 100 ml.) than normal (99 to 127 mg. per 100 ml.) and the rise in blood sugar level was correlated with the increased carbon value. It is suggested that when the residual carbon value increases above normal, a simultaneous increase takes place in non-sugar carbohydrate in the form of " oligosaccharide ", which can be determined as glucose after hydrolysis. In many diabetics this oligosaccharide may substantially supplement the glucose and thus cause the rise in blood sugar level to lag behind the anticipated value. The presence of oligosaccharide in the blood can be eliminated by treatment with either insulin or adrenaline. This hypothesis would account for the observation that the blood sugar values for many diabetics do not correspond to the severity of the illness, and would also explain the lag in response to administration of glucose or insulin. *J. E. Page*

1713. **Vitamin $B_{12}$ Excretion and Diabetic Retinopathy**
B. BECKER, C. A. LANG, and B. F. CHOW. *Journal of Clinical Nutrition* [*J. clin. Nutr.*] **1**, 417–423, Sept.–Oct., 1953. 2 figs., 14 refs.

The amount of vitamin $B_{12}$ excreted in the urine after a single intramuscular injection of 50 or 65 mg. was determined microbiologically and compared in diabetic and non-diabetic subjects at the Hospital for Nutritional Disorders, Mexico City, and in diabetic patients with and without retinopathy at the Johns Hopkins Hospital, Baltimore.

In the first of these experiments 5 diabetic patients were shown to excrete much less of the test dose of vitamin $B_{12}$ than did 9 non-diabetic controls. In the second experiment 22 diabetic patients with retinopathy excreted considerably more of the vitamin than did 13 without retinopathy, their excretion significantly exceeding that of 6 healthy controls. Administration of 100 to 200 mg. of testosterone every 2 or 3 weeks to patients with retinopathy led to a significant decrease in vitamin $B_{12}$ excretion.

Rats treated with cortisone were found to excrete almost twice as much vitamin $B_{12}$ as control animals and animals treated with testosterone. This suggests the possibility that the increased excretion of the vitamin in diabetic retinopathy may be due to excessive corticosteroid production. *K. O. Black*

1714. **Anterior Pituitary Growth Hormone (STH) and Pancreatic Secretion of Glucagon (HGF)**
P. P. FOA, E. B. MAGID, M. D. GLASSMAN, and H. R. WEINSTEIN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **83**, 758–761, Aug.–Sept., 1953. 2 figs., 21 refs.

The diabetes which follows the injection of anterior pituitary extracts has been assumed to result from deficient insulin production due to exhaustion of the beta cells of the islets of Langerhans. An alternative explanation, that anterior pituitary hormones stimulate the alpha cells to increased secretion of glucagon, has been investigated by the authors at the Chicago Medical School.

Cross-circulation experiments were performed on 14 pairs of dogs, the pancreatico-duodenal vein or a mesenteric vein of the donor dog being anastomosed to a femoral vein of the recipient dog. The intravenous injection of pituitary growth hormone into the donor resulted in the liberation of a hyperglycaemic material, presumed to be glucagon, into the blood of the pancreatic vein, causing hyperglycaemia in the recipient dog. Hyperglycaemia did not occur when the recipient received blood from the donor's mesenteric vein, hence the presence of growth hormone itself in the transfused blood could not have been responsible. Thus, in addition to its other known actions, growth hormone seems to cause hyperglycaemia by stimulating the secretion of glucagon. *K. O. Black*

1715. **Selective Destruction of Pancreatic Alpha Cells by Cobaltous Chloride in the Dog. Physiologic Implications**

S. S. LAZARUS, M. G. GOLDNER, and B. W. VOLK. *Metabolism* [*Metabolism*] **2**, 513–520, Nov., 1953. 3 figs., 23 refs.

The authors report experiments carried out at the Jewish Sanitarium, Brooklyn, New York, to elucidate the physiological role of glucagon, the hyperglycaemic, glycogenolytic substance thought to be derived from the alpha cells of the pancreatic islets. An intravenous injection of 200 mg. of cobalt chloride was given as a 1% solution in saline to 30 dogs, some of which were normal, some pancreatectomized, some made diabetic with alloxan, and some partially eviscerated. It was found that within one hour after the injection in normal animals only occasional pancreatic islets still contained intact alpha cells, which in most islets had disappeared or been converted into eosinophilic material. Repeat biopsies on the same animal showed that regeneration of these cells began after 5 days.

A transient hyperglycaemia occurred after the injection in all the animals studied, but the authors conclude that this effect of cobalt is unrelated to its action on the alpha cells. In spite of marked alpha-cell damage there was no subsequent hypoglycaemia, nor was there any amelioration of alloxan diabetes. It is concluded that the alpha cells of the pancreatic islets do not produce any principle influencing carbohydrate metabolism, and that the severity of alloxan diabetes is not related to the presence of the alpha cells. *I. McLean-Baird*

1716. **Renal Vascular Disease in Diabetes Mellitus**

E. T. BELL. *Diabetes* [*Diabetes*] **2**, 376–389, Sept.–Oct., 1953. 13 figs., 18 refs.

In this paper the author reports the changes observed in the renal vessels of 1,465 diabetic patients coming to necropsy at the University of Minnesota Medical School, Minneapolis. It is known that the average severity of atherosclerosis in the renal arteries of diabetics is much greater than in non-diabetics of corresponding age. In the series here reviewed renal atherosclerosis was shown to be rare before the age of 20 (33 patients), but was found in 50% of 234 patients between 20 and 50 years and in two-thirds of those (1,198) over 50, being more frequent in females. When the afferent arteriole was severely affected, there was frequently a less pronounced hyalinization of the efferent arteriole. The involvement of the efferent arteriole appears to be specific for diabetes. Concerning the relationship between arteriosclerosis and hypertension, it was found that a large percentage of diabetics had renal arteriosclerosis but no hypertension, from which it would seem that in these cases the change must be attributed to the diabetic state and not to hypertension. There was, however, an increased incidence of arteriosclerosis in hypertensive diabetics, particularly in subjects under the age of 50, which suggested that in these cases, the hypertension was an additional factor in its causation.

Intercapillary glomerulosclerosis as described by Kimmelstiel and Wilson was found in 19·5% of the male and 30% of the female subjects studied, but was not observed in any subject under 20 years of age. The duration of the diabetes had a striking influence on the development of these lesions in younger diabetics, only 3% of those under 40 years of age and with a history of less than 10 years showing the lesion. It was also shown that intercapillary glomerulosclerosis has a causal relationship to hypertension in subjects under 50 years of age. Proteinuria was present in all subjects with this lesion who were under 50 years of age, but in older subjects it was frequently absent and there was no clear correlation between the amount of protein and the severity of the glomerular change. Similarly, in subjects over 50 there was little correlation between oedema and intercapillary lesions, although in younger subjects the presence of severe oedema was shown to be good evidence of glomerulosclerosis; conversely, patients under 30 and without oedema rarely showed glomerular change.

In the older age group there was some overlapping of renal and cardiac factors causing oedema, but a number of subjects had oedema who had neither renal lesions nor cardiac disease. Hypoproteinaemia was usually found in subjects with oedema, but no close correlation was found between its severity and the degree of oedema. Uraemia was by far the commonest cause of death in subjects with intercapillary glomerulosclerosis, and histological examination of the kidney in these cases showed extensive tubular atrophy, due mainly to obstruction of the glomeruli by intercapillary sclerosis and severe hyalinization of the afferent arterioles. In chronic glomerulonephritis there was rarely hyalinization of afferent arterioles, while in primary hypertension with uraemia the glomerular atrophy was chiefly caused by occlusion of the small renal arteries. These points, the author suggests, serve to differentiate the diabetic kidney with renal insufficiency from chronic glomerulonephritis and primary hypertension with renal insufficiency.

*J. Lister*

1717. **Hepatomegaly and Diabetes Mellitus**

J. I. GOODMAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 1077–1087, Nov., 1953. 46 refs.

A series of 459 diabetic patients (319 male and 140 female) were examined for hepatomegaly by percussion, the distance between the upper and lower borders of the area of liver dullness being measured in the midclavicular line. The upper limit of normal was taken as 7·5 cm. in the male and 7·0 cm. in the female. The patients were classified in three groups according to the state of control of their diabetes: (1) those excreting 50 g. of glucose or less in 24 hours (" controlled "); (2) those excreting more than 50 g. (" uncontrolled "); and (3) those with ketosis. There were 379 patients in Group 1, 33 of whom (9%) had enlargement of the liver; of 70 patients in Group 2, 45 (60%) had enlargement of the liver; and all of the 10 patients with ketosis had marked hepatomegaly.

The author discusses the advantages of percussion over palpation for assessing the size of the liver, and supports the view that hepatic enlargement is a major factor in the production of the abdominal symptoms of diabetic ketosis. *K. O. Black*

# The Rheumatic Diseases

1718. **Some Aspects of the Aetiology of Rheumatic Diseases.** (К вопросу об этиологии ревматической болезни)
E. G. KASSIRSKAYA. *Терапевтический Архив* [*Ter. Arkh.*] **25**, 30–35, Nov.–Dec., 1953. 16 refs.

The negative results of blood culture in many cases of subacute bacterial endocarditis and most cases of rheumatic carditis are due, in the author's opinion, to the fact that the media commonly used do not meet the biological requirements of slow-growing micro-organisms capable of splitting carbohydrates with the formation of acid, since this acid, if allowed to accumulate, soon reaches a lethal concentration.

However, if media which contain natural albumin, such as Löwenthal's broth, semi-liquid agar with plasma, or Tarozzi's medium, are used and the cultures incubated for periods up to 2 months, *Streptococcus viridans* can be isolated in a very much higher proportion of cases. Thus the author was able to isolate *Strep. viridans* in 30 out of 36 cases of subacute bacterial endocarditis (83·3%), in 11 out of 18 cases of primary or recurrent rheumatic carditis (61·1%), and in 17 out of 43 cases of other forms of rheumatism (39·5%).

These findings make it possible to regard all these diseases as of common aetiology. The isolation of the infecting organism is of importance also in the treatment of rheumatic diseases, as by determining its sensitivity the optimum dose of penicillin can be ascertained.

*H. W. Swann*

1719. **Effect of Splenectomy in Acute Systemic Lupus Erythematosus**
H. M. JOHNSON. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **68**, 699–713, Dec., 1953. 3 figs., 27 refs.

The author reports the results of splenectomy in 12 cases of acute systemic lupus erythematosus seen in Hawaii, where the disease is common among the Japanese and Chinese inhabitants. He points out that hypersplenism is the probable cause of the thrombocytopenia, granulocytopenia, and anaemia which are sometimes severe in this disease, and that these haematological manifestations constitute the main indications for splenectomy.

In 2 cases the operation was performed as an emergency for acute thrombocytopenic purpura; after operation there was complete cessation of the haemorrhagic tendency, with dramatic clinical improvement. Anaemia and leucopenia were present in the remaining 10 patients, 2 of whom also had thrombocytopenia, and splenectomy was performed during the active phases of the disease "as a desperate measure". Three of these patients died within 10 days of operation; in the remaining 7 there was a varying degree of symptomatic relief which, however, was maintained in only 2. All but 4 of the 12 patients died from lupus erythematosus within one year of operation; one died 2½ years after operation, but 3 were alive 7, 3, and 2 years later respectively.

The operation was followed by an increase in the erythrocyte, leucocyte, and platelet counts. Histological examination of the spleen, which was enlarged in 8 cases, showed concentric periarteriolar collagen lamination, sinus hyperplasia, and widened marginal zones of medium and large lymphocytes at the periphery of the Malpighian follicles.

(The majority of these cases were seen before the introduction of the L.E.-cell and L.E.-plasma tests, and the diagnosis was based upon the association of fever, polyarthritis, rashes, leucopenia, anaemia, thrombocytopenia, and albuminuria.) *Nigel Compston*

1720. **Effect of Cortisone and Corticotropin on Prognosis of Systemic Lupus Erythematosus. Survey of Eighty-Three Patients with Positive Plasma L.E. Tests**
J. R. HASERICK. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **68**, 714–725, Dec. 1953. 16 refs.

The author describes the natural course of systemic lupus erythematosus in 83 patients seen at the Cleveland Clinic, Cleveland, Ohio, and assesses the results of treatment with cortisone or corticotrophin (steroid therapy) in 73. The series included only those cases in which the L.E. phenomenon was present. The author gives reasons for preferring the L.E.-plasma test to the L.E.-cell test; he considers that the former is as specific in the diagnosis of systemic lupus erythematosus as the Wassermann test in the diagnosis of syphilis. He points out that before the introduction of the L.E.-plasma test a diagnosis of systemic lupus erythematosus was made only in typical, severe cases. Since then milder, atypical forms of the disease have been recognized, and when these are included in any series of cases the over-all prognosis is improved. A comparison of statistics of cases diagnosed by the L.E.-plasma test with those of cases diagnosed clinically is therefore invalid.

The course of lupus erythematosus in 10 patients treated before steroid therapy was available is compared with that in 73 given cortisone or corticotrophin. The initial and maintenance doses are not given.) The author's criterion of effective therapy is the survival of those patients "considered to have imminently fatal systemic lupus erythematosus". Only one of the 10 untreated patients was alive 5 years after the onset of the severe phase; the remainder died one month to one year after onset. Of the treated patients, 44 were expected to die and steroid therapy is considered to have prevented death in 30 of these. A number of deaths occurred within a few days of the start of treatment. In 4 cases renal failure was progressive in spite of treatment. Of 11 patients given steroid therapy in 1949 and 1950, 7 were alive in 1953. Not only was life prolonged by these drugs, but morbidity was reduced.

(In the discussion which followed, the author discussed the false positive response to the L.E.-plasma test, which is sometimes noted in patients reacting to penicillin. Such responses were " very low-grade positive ", only a small number of cells undergoing the characteristic changes. In systemic lupus erythematosus the reactions were always strongly positive.) *Nigel Compston*

1721. **Pulmonary Lesions of Disseminated Lupus Erythematosus**

S. I. RAPAPORT, L. MEISTER, F. M. STEELE, and S. R. CANIGLIA. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 268–274, Dec., 1953. 5 figs., 19 refs.

Although the pleural reactions in disseminated lupus erythematosus are well recognized, many published accounts of the visceral lesions fail to mention the lung parenchyma or to distinguish between primary involvement and a secondary infective pneumonia, usually manifested as recurrent bouts of bronchopneumonia. The primary pulmonary lesions, although frequent, are often atypical; they are usually asymptomatic, and are seen radiologically as diffuse infiltration or as massive consolidation or atelectasis. The commonest lesion is a patchy, shifting area of pneumonitis at the base of the lung, associated with a pleural reaction.

The present authors describe in detail 2 cases of disseminated lupus erythematosus with primary pulmonary lesions admitted to the Veterans Administration Hospital, Long Beach, California. A man of 44 had a cough, with mucoid sputum which later became dry, pleurisy, and fever. The chest radiograph showed bilateral pneumonitis with some, mainly basal, pleural exudate. There was little change in the radiograph over a period of 7 months, though there was some diminution in density of pneumonitis. Within 24 hours of the start of ACTH therapy considerable symptomatic improvement was observed, and by the 67th day the chest radiograph was clear. The patient was still in remission 2 months later. The absence of purulent sputum suggested primary disease rather than long-standing bilateral pneumonia. Although certain other features of the disease were present the pulmonary lesion dominated the picture.

The second patient, a man of 35, had painful swelling of the fingers and toes but no chest symptoms. The radiograph showed a streaky, mottled infiltration throughout both lower lung fields which was interpreted as bilateral pneumonitis. A 10-week course of ACTH produced improvement in the joints, but there was no change in the chest radiograph over a period of one year, during which time he had no respiratory symptoms and no pleural reaction. *A. Gordon Beckett*

1722. **Phenylbutazone Therapy. Relation between the Toxic and Therapeutic Effects and the Blood Level**

E. BRUCK, M. E. FEARNLEY, I. MEANOCK, and H. PATLEY. *Lancet* [*Lancet*] **1**, 225–228, Jan. 30, 1954. 2 figs., 12 refs.

The relation between the blood level of phenylbutazone given by mouth and the toxic and therapeutic effects was investigated at the West London Hospital, Hammersmith, in 52 patients, 48 of whom had rheumatoid arthritis and 4 had osteoarthritis.

The blood level of phenylbutazone varied considerably in different patients on the same daily dosage. The average level, however, rose steadily when the dosage was increased up to 600 mg. daily; when it was increased beyond this to a maximum of 1,200 mg. the blood level rose less quickly. Toxic effects were noted in 25 patients, but were mild in 15 and did not call for cessation of treatment. There was a marked and statistically significant correlation between the incidence of side-effects and the blood level of the drug; when the blood level of phenylbutazone was more than 10 mg. per 100 ml. the incidence of side-effects was high (85%). One patient died from renal failure, possibly precipitated by the salt-retaining effect of phenylbutazone.

No objective improvement was observed in any of the patients, and the authors therefore had to rely on the subjective response to assess the therapeutic effect of the drug. On this basis they found that when the blood level was below 5 mg. per 100 ml., 2 out of 8 patients obtained relief of symptoms; when the level was between 5 mg. and 10 mg. per 100 ml., 25 out of 29 patients experience relief of symptoms. At blood levels above 10 mg. per 100 ml. the therapeutic effect was not notably enhanced.

In another investigation the authors found that the blood level of phenylbutazone rose slowly, reaching a maximum in about 10 days. The drug was retained in the body, and when administration ceased excretion continued for 10 to 21 days. Toxic effects may therefore persist or may even appear after the drug has been discontinued.

The authors consider that phenylbutazone is most effective at a blood level of 5 to 10 mg. per 100 ml., but because of individual variations in absorption a fixed scheme of dosage cannot be laid down. They suggest that a dose of 200 mg. daily should be given initially, increasing by 100 mg. daily until the response is satisfactory. With doses of more than 400 mg. daily the likelihood of serious toxic reactions increases rapidly.
*B. E. W. Mace*

1723. **Locally Administered Hydrocortisone in the Rheumatic Diseases. A Summary of its Use in 547 Patients**

E. M. BROWN, J. B. FRAIN, L. UDELL, and J. L. HOLLANDER. *American Journal of Medicine* [*Amer. J. Med.*] **15**, 656–665, Nov., 1953. 1 fig., 19 refs.

Over a period of 18 months at the Hospital of the University of Pennsylvania, Philadelphia, 547 patients with rheumatic disease received injections of hydrocortisone into inflamed joints or bursae, the total number of injections being 3,757. Of the 547 patients, 249 had rheumatoid arthritis, 231 had osteoarthritis, 18 had gout, and 49 had various rheumatic conditions (details given).

The dose of hydrocortisone ranged from 5 to 50 mg. according to the size of the joint and the result obtained. Results were assessed both symptomatically and by the size and range of movement of the joint. Many of the patients with rheumatoid arthritis were receiving systemic treatment (cortisone or gold, or both) so that the results were difficult to assess, but it is considered that " satisfactory " improvement occurred in 85% of the patients

treated. Those with osteoarthritis of the hip were noticeably resistant to treatment, possibly because of the technical difficulty of injection into this joint. Reactions, which occurred after 2·3% of the injections, included transient local exacerbation of inflammation, weakness of a limb, general malaise, urticaria, and in one case infection of the joint.

It is concluded that intra-articular injection of hydrocortisone is a useful adjuvant in the general treatment of rheumatoid arthritis, osteoarthritis, gout, and various local rheumatic disorders. *Kathleen M. Lawther*

1724. **Liver Biopsy in Rheumatoid Arthritis**
E. R. MOVITT and A. E. DAVIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **226**, 516–520, Nov., 1953. 13 refs.

It has been suggested by Archer (*Ann. intern. Med.*, 1951, **34**, 1173) that the impairment of hepatic function frequently reported to occur in rheumatoid arthritis may well be due to the therapeutic agents commonly employed, many of which are hepatotoxic. The present authors describe their findings in 17 cases of rheumatoid arthritis in men who were subjected to needle-biopsy of the liver and various tests of hepatic function. They found no significant evidence of hepatic damage, even when the disease was of many years' standing. *A. C. Lendrum*

1725. **The Treatment of Periarthritis of the Shoulder with Hydrocortisone Acetate.** (Le traitement de la périarthrite de l'épaule par l'hydrocortisone acétate)
A. ROBECCHI and R. CAPRA. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **20**, 757–763, Nov., 1953.

After commenting on the great variety of treatment which has been advocated for periarthritis of the shoulder the authors maintain that whereas cortisone gives results which are in no way superior to simpler, cheaper, and less dangerous forms of therapy, hydrocortisone on the other hand gives excellent results on local injection and is the treatment of choice. Of 50 cases so treated at the Turin Rheumatological Centre, in 20 (58 injections) the condition was acute, in 14 (38 injections) it was chronic but without fixation of the joint, and in 16 (58 injections) the joint was more or less "frozen". Hydrocortisone was injected, so far as possible, in the region of affected tendons or of the subacromial bursa, but in a few intractable cases it was given intra-articularly. The usual dosage was 25 mg. (1 ml.), and an interval of 3 to 5 days was allowed between injections.

The best results were obtained in acute cases, where rapid relief from pain was experienced in all but one case, the final result being classified as "good" or "very good" in 16 out of 20. A similar degree of relief of pain was obtained in 7 out of the 14 chronic non-rigid cases, and in 7 out of the 16 cases with rigidity. Stiffness and immobility, however, appeared to be uninfluenced and required physical methods of treatment, which the relief of pain greatly facilitated. There was some evidence that calcification, when present, was more rapidly absorbed after treatment with hydrocortisone than is usually the case in spontaneous remissions. In the opinion of the authors, the radio-opaque appearances in such cases are due to subacromial bursitis, the fluid being rich in calcium salts. *D. Preiskel*

1726. **Determination of C-reactive Protein in Serum as a Guide to the Treatment and Management of Rheumatic Fever**
G. H. STOLLERMAN, S. GLICK, D. J. PATEL, I. HIRSCHFELD, and J. H. RUSOFF. *American Journal of Medicine* [*Amer. J. Med.*] **15**, 645–655, Nov., 1953. 6 figs., 12 refs.

Tests for the presence of C-reactive protein (C.R.P.) in the serum of 62 patients with rheumatic fever were carried out at Irvington House (New York University College of Medicine), the patients being grouped according to the stage of rheumatic activity as follows: (1) active rheumatic fever, 35 patients; (2) low-grade rheumatic activity, 11; (3) "doubtful activity", 11; and (4) "pure chorea", 5. Observations were continued during treatment with various antirheumatic agents (including ACTH and cortisone) and during 6 months' convalescence. C.R.P. was present in the blood in nearly all the clinically active cases and in 6 of the 11 doubtful cases, but was absent in all 5 cases of "pure chorea". Disappearance of C.R.P. from the blood is believed to indicate the termination of a rheumatic attack, while persistence of C.R.P. during treatment indicates inadequate suppression of the inflammatory process.

It is concluded that the presence of C.R.P. in the blood of a rheumatic patient is an extremely sensitive and reliable indication of rheumatic activity, but it is emphasized that its appearance is a non-specific response to many inflammatory processes. In certain isolated rheumatic conditions—for example, chorea, erythema marginatum, and subcutaneous nodules—there may be no C.R.P. in the patient's blood. *Kathleen M. Lawther*

1727. **Epidemiology of Rheumatic Fever in a Rural District in Italy with Particular Reference to Some Environmental Factors**
A. POPPI, G. LABO, G. LENZI, and L. ROSA. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 310–314, Dec., 1953. 1 fig., 7 refs.

The incidence of rheumatic fever among women workers in a region in the lower Po valley was studied at the University of Bologna. A total of 930 apparently fit women aged 14 to 70 years were examined, of whom 607 were employed in the rice fields and the remainder (323) in other occupations. It was found 24·3% of the rice workers and 6·8% of those engaged in other occupations had a definite history of rheumatic fever, while 11·3% of the rice workers and 2·8% of the remainder had rheumatic heart disease. It is believed that this high incidence is related to the damp climate, poor housing conditions, and an unsatisfactory diet (consisting chiefly of carbohydrates), and that the type of employment is an important aetiological factor. The rice workers stand long hours in water under considerable physical strain; most of them migrate seasonally into the rice area where they are housed in barracks, which are overcrowded and badly ventilated. *K. C. Robinson*

# Neurology and Neurosurgery

1728. **Anencephalus, Spina Bifida, and Hydrocephalus. Incidence Related to Sex, Race, and Season of Birth, and Incidence in Siblings**
B. MACMAHON, T. F. PUGH, and T. H. INGALLS. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **7**, 211–219, Oct., 1953. 1 fig., 21 refs.

This study is based on the incidence of major congenital abnormalities of the central nervous system—anencephalus, spina bifida, and hydrocephalus—among the 168,654 births in five maternity hospitals in the State of Rhode Island between 1936 and 1952, approximately 70% of all births in the area taking place in these hospitals.

The total number of such cases was 904, the incidence per 1,000 births being 1·93 for anencephalus, 2·53 for spina bifida, and 0·90 for hydrocephalus. The total incidence of these abnormalities reached a peak in 1942 and has declined since. There was a female preponderance among cases of anencephalus and spina bifida and a male preponderance among cases of hydrocephalus. There was a higher incidence of hydrocephalus among negroes and of anencephalus and spina bifida among whites, and a strikingly low incidence of all three malformations among Jews. No seasonal difference in the incidence of anencephalus was found, in contrast to the findings of McKeown and Record (*Lancet*, 1951, **1**, 192; *Abstracts of World Medicine*, 1951, **10**, 3) in Birmingham, England, where there was a higher incidence among infants born between October and March. Information on the proportion of children with malformations of the central nervous system among those born to the same parents after the index case is reported for one of the maternity hospitals. Here the incidence of malformation was 6 in 119 for anencephalus, 11 in 166 for spina bifida, and 1 in 54 for hydrocephalus. These figures are of the same order as those found in the Birmingham survey, though somewhat higher. It was confirmed that anencephalus and spina bifida, but not hydrocephalus, tend to occur in the same fraternity and therefore probably have a common aetiology. *C. O. Carter*

## BRAIN AND MENINGES

1729. **Complications Following Cerebral Angiography**
D. M. PERESE, W. C. KITE, A. J. BEDELL, and E. CAMPBELL. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **71**, 105–115, Jan., 1954. 3 figs., 26 refs.

The complications following the performance of carotid arteriography on 234 consecutive occasions in 200 cases are reviewed. Diodone in 35% solution was injected percutaneously on 201 occasions and on 33 the artery was exposed by open operation, the total amount injected at each session varying between 10 and 60 ml., and averaging 30 ml. given in 3 injections of 10 ml. Local analgesia with 1% procaine hydrochloride was used in 70% of cases, and in the remaining 30%, thiopentone or nitrous oxide was employed.

There was one death directly attributable to arteriography and in 6 other cases death was hastened by the procedure. Transient hemiplegia occurred in 19 cases, and permanent hemiplegia in 3. A retinal artery was occluded on one occasion, and in 2 cases a haematoma had to be evacuated from the neck. Detailed accounts of the 7 fatal cases and the case of the occluded retinal artery are given.

The authors consider that the maximum amount of diodone injected at a single sitting should not exceed 30 ml. The various factors which may be responsible for the neurological complications are discussed; these include the formation of a " clot embolus ", the rupture of an aneurysm due to sudden increased intravascular pressure attendant on the injection, and alteration in the blood–brain barrier due to the toxicity of the medium.

[Carotid arteriography is undoubtedly a potentially dangerous procedure, but the incidence of complications in this series of cases (just over 14%) seems unduly high compared with the experience of others.

The authors are, in the abstracter's opinion, overcautious in recommending that not more than 30 ml. of diodone should be used at one sitting, though obviously the less used the better. Other possible factors in the causation of complications are the use of the open method of arteriography, in which there are very real dangers of " clot-embolus " formation and secondary infection in the wound, and the use of general anaesthesia preventing the cooperation of the patient, who may give early warning of impending disaster.] *W. B. D. Maile*

1730. **The Confluence of Dural Venous Sinuses**
H. BROWNING. *American Journal of Anatomy* [*Amer. J. Anat.*] **93**, 307–329, Nov., 1953. 5 figs., 29 refs.

The material for the study here reported from Yale University School of Medicine and Indiana University Medical School was obtained from 100 adults after embalming (in 50 cases at necropsy and in 50 from the dissecting room). The dura of the posterior fossa was removed and the cross-sectional areas of the superior sagittal, straight, and transverse sinuses 5 cm. from their confluence were calculated. In 30 of the necropsy specimens the outflow through each transverse sinus of fluid entering through the superior sagittal or the straight sinus, or both together, at a pressure of 60 cm. of water was measured. Dissections of the systems, were made, and in 37 cases the pattern was compared with the bony markings on the skull.

There were four main types of confluence. In Type 1 (36%) all four sinuses met in a common pool and in Type 2 (24%) the superior sagittal and straight sinuses were both bifurcated, each transverse sinus receiving a branch from each of the others, whereas in Type 3 (24%) only the straight sinus and in Type 4 (16%) only the

superior sagittal sinus was bifurcated. Minor variations included the placing of the superior sagittal or straight sinuses to one side of the midline and the presence of small ridges of dura and of small anastomotic channels between different portions of the confluence. In 20% of cases there was no evidence of the dominance of one transverse sinus over the other, while in 29% there was left and in 51% right dominance. The occipital sinuses showed much variation and were comparatively small, except in 9 cases in which their combined capacity was similar to that of the straight sinus. In 43% of the cases examined there was no correlation between sinus capacity and the dimensions of their bony markings. In the perfusion experiments the total outflow with all sinuses open ranged from 522 ml. to 952 ml. per minute. When one transverse sinus was occluded, the remaining sinus could, in most cases, accommodate the total outflow, but when one transverse sinus had more than three times the capacity of the other (" major dominance "), occlusion of the larger sinus led to a deficiency of 20 to 74% in total outflow. In all cases there was found to be some mixing at the confluence.

The author's findings are compared with those of other investigators and their practical significance in relation to operations for the revascularization of the brain and to ligation of the internal jugular vein is discussed.

*D. B. Moffat*

1731. **The Psychosurgery of Intractable Pain. A Study of 57 Cases.** (La psychochirurgie des algies irréductibles. Étude basée sur 57 cas)
D. PETIT-DUTAILLIS, R. MESSIMY, and L. BERGES. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **29**, 3893–3903, Dec. 6, 1953. Bibliography.

In the 57 cases here reported from the Neurosurgical Clinic, Hôpital de la Pitié, Paris, various operations were performed on the frontal cerebral lobes in an attempt to relieve intractable pain that could not be otherwise treated. In all cases the authors were careful to limit the amount of cerebral tissue destroyed, in order to preserve as far as possible the patient's personality unchanged. The indications for operation were those generally accepted for this type of operation. The largest group consisted of patients with visceral cancer in whom posterior-root section or cordotomy were contraindicated, another group was formed by patients with various types of facial hyperalgia, while the remainder included a number of cases of intractable pain in amputation stumps, brachial plexus hyperalgia, thalamic syndromes, and a few with tabes dorsalis. In 7 cases resection of only a limited area of cortex (topectomy) involving Brodmann's areas 9, 10, 45, and 46 was carried out. Of the remaining 50 patients, 23 underwent a large bilateral frontal lobectomy, performed in all but one case at the site of election under vision after exposing the frontal lobes from above, 7 bilateral lobectomy in 2 stages, and in 20 cases only a unilateral lobectomy was performed. The results of follow-up for various periods (in many cases to death) showed that only bilateral lobectomy gave satisfactory relief of pain, and that this was in most cases accompanied by some disorder of personality of varying degree. Left unilateral lobectomy also gave good relief in a few cases but was also accompanied by personality disorders which, however, were thought to be less persistent than in the patients bilaterally treated. The two-stage operation is not recommended. Topectomy gave disappointing results. It is concluded that for relief of intractable pain by surgical means, bilateral lobectomy gives the best results but that in many cases a considerable risk of change in personality must be accepted. *Donald McDonald*

1732. **Stimulation of the Hippocampus and Medial Cortical Areas in Unanesthetized Cats**
B. R. KAADA, J. JANSEN, and P. ANDERSEN. *Neurology* [*Neurology*] **3**, 844–857, Nov., 1953. 7 figs., 38 refs.

Recent work has thrown doubt on the concept, hitherto generally held, of the purely olfactory function of the forebrain. The authors have therefore, at the Anatomical Institute, University of Oslo, further studied the results of stimulation of the hippocampus and other forebrain structures by means of implanted electrodes in unanaesthetized cats.

Stimulation of the hippocampus and fimbria of the fornix resulted in an attitude of alertness, the cat turning its head and eyes to the opposite side in anxious searching movements, but seeming to direct its attention to a hallucination or some psychical experience and never to its own body, as may happen when the amygdaloid nucleus is stimulated. There was no rhythmical sniffing or licking and, apart from slow pupillary dilatation, there were no autonomic effects. During the period of stimulation the animal remained conscious, but its reaction to external stimuli was diminished. The response to stimulation of a given point was stereotyped, and was fairly uniform during prolonged stimulation. Stronger stimuli accelerated the glancing or circling movements and sometimes evoked fear or anger, especially if the animal was touched or restrained. The authors draw attention to the similarity between these movements and those often seen in cases of psychomotor epilepsy.

The finding that stimulation of the proreate, limbic, and hippocampal gyri had almost the same result as had stimulation of the hippocampus and fimbria is consistent with the fact that these structures, together with the mammillary body and the anterior nucleus of the thalamus, constitute a circular pathway. On the whole, fear or anger were less evident when the anterior limbic area was stimulated. The results of preliminary ablation experiments followed by stimulation suggest that the response does not depend upon the integrity of the cingulum, but is mediated by projections from the various areas to common subcortical structures. *J. Foley*

1733. **Experimental Intracisternal Injection of Polymyxin B. Its Role in the Treatment of Septic Meningitis**
P. TENG and B. A. JOHNSON. *Neurology* [*Neurology*] **3**, 831–843, Nov., 1953. 2 figs., 12 refs.

The authors recall that the toxicity of antibiotics for the central nervous system does not run parallel with their general toxicity. In experiments carried out at Mount Sinai Hospital, New York, they found that poly-

myxin B is both irritant and toxic when injected intrathecally, particularly in animals, 3 of their experimental dogs dying after injections of 40,000 units. Smaller doses caused weakness of the hind legs, and when the animals were killed a month later, chromatolysis of some anterior horn cells and demyelination of the peripheral parts of the spinal cord were found.

Two clinical cases of bacterial meningitis are also described. In the first, a newborn infant with meningitis due to *Bacterium coli*, the administration of 5 mg. (50,000 units) of polymyxin B, which was tried after other antibiotics had failed, caused convulsions. The spinal fluid was, however, rendered sterile, and the infant eventually made a good recovery. The second case occurred in a 29-year-old man with otogenic meningitis due to mixed organisms; an intrathecal injection of 50,000 units of polymyxin B caused backache and retention of urine for 5 days. This patient also recovered. The authors recommend that the intrathecal dose of polymyxin B should not exceed 1,000 units in a baby, 5,000 units in a child under 5 years, and 15,000 units in an adult.

[In reviewing the toxic effects of polymyxin on the nervous system in cases of septic meningitis collected from the literature, the authors do not distinguish between polymyxin B and polymyxin E.] *J. Foley*

1734. **Studies of the Mode of Action of Apomorphine on the Tremor of Parkinsonism.** (Untersuchungen über die Wirkungsweise des Apomorphin auf den Parkinsontremor)
A. STRUPPLER and T. VON UEXKULL. *Zeitschrift für klinische Medizin* [*Z. klin. Med.*] **152**, 46–57, 1953. 3 figs., 23 refs.

The authors found that apomorphine given in daily doses of 0·5 to 0·75 mg. intramuscularly or 300 to 450 mg. by mouth considerably reduced the tremor in 12 cases of Parkinsonism treated at the University Medical Clinic, Munich. The rigidity was little affected. The drug in these amounts did not produce nausea or vomiting. In the course of investigation of the nature of this action of the drug it was shown that vestibular stimulation, calorically or by rotational movement, could also reduce the tremor. The tremor of Parkinsonism is believed to be due to the involvement of the mechanism which anticipates the positioning of limbs (not quite the same as an intention tremor), and it is upon this mechanism that apomorphine is thought to act.

*G. S. Crockett*

## CEREBRAL VASCULAR DISORDERS

1735. **Cerebral Hemodynamics and Metabolism in Subjects over 90 Years of Age**
J. F. FAZEKAS, J. KLEH, and L. WITKIN. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **1**, 836–839, Dec., 1953. 8 refs.

The cerebral blood flow and cerebral metabolism were studied at the Gallinger Municipal Hospital and the Home for the Aged and Infirm, Washington, D.C., in 18 patients between 90 and 102 years of age. The cerebral blood flow was determined by the method of Kety and Schmidt as modified by Scheinberg and Stead. The mean values for cerebral blood flow and cerebral metabolic rate in these patients were significantly lower than those in normal subjects under 50 years old, but not significantly different from those in normal subjects over 50. The variation between individuals was wide, and the correlation between cerebral blood flow and cerebral metabolism in individual cases was poor. It was impossible to determine from these results whether the reduced metabolism was due to vascular insufficiency or primary cellular disturbance. Similar variations with age have been observed in rats, which do not develop arteriosclerosis. It is suggested that there is no relation between cerebral blood flow and mental status (which in the authors' cases was either "alert" or "senile", except in one patient who was semicomatose).

*J. N. Agate*

1736. **Concerning Injuries, Aneurysms and Tumours Involving the Cavernous Sinus**
G. JEFFERSON. *Transactions of the Ophthalmological Society of the United Kingdom* [*Trans. ophthal. Soc. U.K.*] **73**, 117–152, 1953. 11 figs., 45 refs.

This paper (constituting the text of the Bowman Lecture for 1953) is based on the author's experience in 112 cases of lesions of the cavernous sinus, all of which were verified pathologically, with particular reference to their ocular manifestations. The clinical material is classified as follows. (A) Traumatic; 22 cases, of which 5 showed ophthalmoplegia alone and 17 nerve lesions associated with carotico-cavernous fistulae; isolated abducens palsy (12) was the most common form of ophthalmoplegia in the latter group, in which involvement of the third or fourth nerve alone was not seen. (B) Aneurysms; 38 cases, of which 29 were saccular and 9 had formed spontaneous fistulae. (C) Tumours involving the cavernous sinus; 52 cases.

The author agrees with Cross that in most cases ocular palsy appearing after head injury is unrelated to damage to the cavernous sinus and is due to intra-orbital damage: the most certain sign of injury to the sinus is multiple oculomotor involvement, usually of all the nerves and commonly associated with a trigeminal lesion. Pulsating exophthalmos resulting from rupture of an injured artery within the cavernous sinus was less common in the author's series than it is generally thought to be, and when it did appear it was more often due to involvement of the orbital veins in the pathological process. The one characteristic feature of an arterio-venous fistula is the bruit, but this may not become apparent, even in conscious patients, for some weeks after the injury, suggesting delayed rupture of a traumatic aneurysm. Ophthalmoplegia in such cases is often variable and inconstant, and is less likely to be due to direct pressure within the sinus than to secondary orbital changes resulting from the reversal of orbital circulation.

Aneurysms within the cavernous sinus are most commonly found in females of middle age and over; only 4 of the author's 38 cases were in males and all but 4 of the patients were over 50. Their site within the sinus is reliably indicated by the degree of trigeminal involvement,

and " the presence of [unimpaired] corneal sensation can be taken as an absolute criterion of normality ". Angiography is an invaluable diagnostic aid, but does not necessarily indicate the full extent of the aneurysm. Ophthalmoplegia is frequent and, like the other signs and symptoms of aneurysm, commonly transient. Primary tumours of the sinus wall or of its contained structures are rare and accounted for only 7 of the 52 cases in this group. Invasion by malignant naso-pharyngeal tumours was the most frequent cause (23 cases), and invasive pituitary adenomata (11) and carcinomatous metastases (8) accounted for most of the remainder. A sudden onset with severe pain suggestive of a saccular aneurysm is not uncommon with both primary and secondary tumours, but in the case of pituitary tumours the appearance of characteristic endocrine signs may be long delayed. Ophthalmoplegia in such cases is more likely to result from local pressure than from invasion of the nerve. The anatomical and pathological background of the complex aural, nasal, cervical, and neuro-ophthalmological signs and symptoms of these tumours is discussed in detail by the author, who emphasizes especially that involvement of the cervical lymph nodes is an important factor in their differentiation from meningiomata, and that involvement of the optic nerve occurs much more commonly with invasive tumours than with aneurysms.

[The paper is liberally illustrated with case histories and angiograms and forms an invaluable reference survey which should be consulted directly for further detail.]

*H. E. Hobbs*

1737. **The Treatment of Chronic Subdural Haematoma. A Study of 31 Personal Cases.** (Traitement de l'hématome sous-dural chronique. Étude de 31 observations personnelles)

D. PHILIPPIDES, B. MONTRIEUL, and R. STEIMLÉ. *Journal de chirurgie* [*J. Chir.* (*Paris*)] **69**, 947–960, Dec., 1953. 4 figs., bibliography.

In this paper from the Faculty of Medicine, Strasbourg, an analysis is made of 31 cases of chronic subdural haematoma treated by the authors. After a brief review of the operative procedures employed by previous workers for obliteration of the space left after evacuation of the haematoma, attention is drawn to a condition of active hypotension, superimposed upon the passive hypotension due to the compression, which may occur in the dehydrated and hypotonic cerebral tissue. In such a condition the cerebral hemisphere will not expand after a long period of compression, and the cavity previously occupied by the haematoma fills up either with serum or with a fresh extravasation of blood. The patient again falls into coma, the temperature and tension rise, and paresis of the opposite side may occur. The picture of this serious condition is easily confused with that of intracranial hypertension.

For recent haematomata with a history of 6 to 8 weeks and with fluid contents and a thin capsule, the authors perform evacuation by a single trephine hole in the parieto-occipital region and, if the tumour be very large, by a second opening in the occipital region. After lavage with physiological saline solution, drainage is established for 2 or 3 days. In the authors' series of 21 such cases there were 2 deaths. In cases in which the capsule is thick, and especially when its inner layer is adherent to the cerebral cortex and so preventing the expansion of the compressed hemisphere, as complete a removal as possible of the capsule of the haematoma is effected by a large fronto-parietal osteoplastic flap. In 10 of these cases one patient died. If the edges of the capsule, especially near the sagittal sinus, will not come away easily, they may be left. A large flap allows all bleeding points to be adequately dealt with.

After operation, collapse of the cortex is dealt with, and expansion encouraged, by injection of saline solution either into the unaffected ventricle or into the subarachnoid space by spinal injection with the patient in the Trendelenburg position. A constant watch must be maintained during convalescence. The progressive onset of coma necessitates immediate investigation of the intraventricular and lumbar pressures and, if these show the existence of hypotension, treatment must be carried out by injection of physiological saline, which should also be given intravenously.

Arteriography, and to a less extent electroencephalography, are valuable in diagnosis and as a postoperative means of detecting signs of the two major complications, namely, cerebral collapse and re-establishment of the haematoma. Analysis of the follow-up results showed that 15 out of the 19 surviving patients undergoing simple drainage were completely cured, 2 have died of intercurrent affections, one is no longer working, and one has residual paresis of the right leg. Of the 9 surviving patients who underwent removal of the capsule of the haematoma, all have been able to return to work.

*D. P. McDonald*

## CEREBRAL TUMOURS

1738. **Figure-ground Discrimination and the " Abstract Attitude " in Patients with Cerebral Neoplasms**

W. S. BATTERSBY, H. P. KRIEGER, M. POLLACK, and M. B. BENDER. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **70**, 703–712, Dec., 1953. 2 figs., 34 refs.

At Mount Sinai Hospital, New York, 40 patients undergoing operation for supratentorial cerebral tumour were studied both pre- and post-operatively for signs of deterioration in intellectual capacity. Each was given a battery of tests consisting of a modified form of Gottschaldt's " hidden figures " test, a Weigl type of sorting test, and the Wechsler–Bellevue Form I. The patients were grouped according to site of the tumour into those with pre-Rolandic, post-Rolandic, and intermediately placed tumours. A control group consisting of 24 patients with raised intracranial pressure due to lesions other than supratentorial tumours were also tested.

Patients with tumours of the hemisphere showed defective performance in all three tests, although the degree of defect was less than the authors had expected from a study of the literature. " Concreteness " was

frequently evident. No significant difference could be found in the incidence and severity of the defect between the three subgroups of patients with supratentorial tumours. At times the defect appeared to be due to perseveration rather than a failure of " abstract thinking ", for the patient might express knowledge of the alternatives and yet use only one of them. Patients in the control group (with posterior-fossa tumours) gave a better performance than those with hemisphere tumours.

The authors conclude that the so-called " intellectual " defects supposedly specific to frontal-lobe lesions either do not exist or are of such a nature that the tests used in this study were inappropriate for their detection.

*L. G. Kiloh*

1739. **Hypoglycorrhachia of Non-Infectious Origin: Diffuse Meningeal Neoplasia**

L. BERG. *Neurology* [*Neurology*] **3**, 811–824, Nov., 1953. 8 figs., bibliography.

The sugar content of the cerebrospinal fluid (C.S.F.) may be lowered in a number of conditions, such as bacterial meningitis, hypoglycaemia, after subarachnoid haemorrhage (rarely), and in diffuse infiltration of the meninges with malignant cells of carcinoma, glioblastoma, lymphosarcoma, or melanoma, while it has also been reported in sarcoidosis of the meninges. Accelerated glycolysis by the malignant cells is thought to be the most likely explanation in the diffuse neoplastic cases.

In this paper the author describes 3 interesting cases of gliomatosis, in 2 of which there was a diminished sugar content in the C.S.F., and also 2 cases of disseminated lymphosarcoma studied at the Presbyterian Hospital, New York (Columbia University). In a review of the literature he found that a low C.S.F. sugar content was present in 75% of 57 reported cases of diffuse meningeal neoplasia.

*J. Foley*

## EPILEPSY

1740. **Diagnosis and Prognosis of Hypsarhythmia and Infantile Spasms**

E. L. GIBBS, M. M. FLEMING, and F. A. GIBBS. *Pediatrics* [*Pediatrics*] **13**, 66–73, Jan., 1954. 4 figs., 2 refs.

The authors describe a series of 237 cases, observed at the University of Illinois College of Medicine, Chicago, during the course of routine electroencephalographic studies of epileptic patients, in which there was a peculiar type of electroencephalographic pattern characterized by very high voltage and random slow waves and spikes in all cortical areas. It could be distinguished from the petit-mal or petit-mal-variant pattern by the lack of any organized or repetitive rhythms, and occurred most often in young infants, 160 of the patients being under one year and most of the rest being under 2 years of age. It was rarely observed after 4 years of age.

Clinically, these patients showed sudden jerking of the head, rolling of the eyes, upward flinging of the arms, or quivering of the body. Although abrupt and short, the attacks were longer than those of myoclonic epilepsy. Of the children over one year old, 87% were mentally retarded and 63% showed some degree of motor impairment. Cerebral palsies were present in 25% and infections, chiefly encephalitis, in 18%, but in 55% there was no obvious cause. The condition tends to clear up with increasing age, but in a follow-up study of 103 cases 11 (10·7%) were reported to be dead before the 3rd year; in the survivors the mental defect remains.

The condition is little influenced by anti-epileptic drugs, but encouraging results are reported from the use of antibiotics, the administration of large doses of aureomycin, oxytetracycline, or chloramphenicol for 10 to 20 days being the treatment of choice.

[It is a little unclear as to whether the authors regard this condition as symptomatic or primary. No details are given of any clinical or pathological investigations and no mention is made of post-mortem examination of any of the patients who died. If this condition is, in fact, a true disease entity with 10% mortality and a 90% chance of mental impairment, it would seem to justify a rather more comprehensive and detailed treatment than it receives in this paper.]

*N. S. Alcock*

1741. **Primidone (Mysoline) in the Treatment of Clinical Petit Mal in Children**

J. N. BRIGGS and J. TUCKER. *Lancet* [*Lancet*] **1**, 19–21, Jan. 2, 1954. 6 refs.

From the Children's Hospital and University of Sheffield the authors report the treatment of 22 cases of petit mal, with or without grand mal, with primidone (" mysoline "). Of the 22 patients, 19 were already under treatment, but the epilepsy was not satisfactorily controlled by drug therapy, and 3 received primidone from the start of their illness. Epilepsy was diagnosed clinically, but an electroencephalogram (EEG) was taken in all cases at some stage during the investigation. Petit mal was present alone in 13 cases and with grand mal in 9. Primidone was the only anti-epileptic drug administered, except in one case in which phenobarbitone was also given.

The dose of primidone at the start of treatment was 0·125 g. a day for children under 5 years and 0·25 g. a day for those over 5. The initial dose was given in the evening; thereafter the drug was given twice daily. Immediate response to these low doses was unusual, the attacks in most cases becoming more frequent, so that the dosage had to be increased fairly rapidly to 0·5 g. daily. If this was insufficient to control the attacks, a further 0·25 g. a day was added at fortnightly intervals until they were completely controlled. If toxic symptoms developed, the dose was usually reduced by 0·25 g. The highest dosage was 1·5 g. per day; most of the older children required about 1·0 g. per day.

After at least one year's treatment the condition of the patients was: "much improved" in 7; " improved " in 7; unchanged or worse in 8. The major fits were completely controlled in 7 of the 9 children with associated grand-mal epilepsy. Troxidone had been given to 14 of the patients before the start of this investigation, and a comparison of the results with those obtained with primidone showed that in 7 the attacks were " definitely better " with primidone, in 5 neither drug was of value, and in 2 troxidone was the more effective drug.

There was no fundamental difference between the EEG of those patients who responded to primidone and the EEG of those who did not; nor was there any fundamental change when the patient was not receiving the drug, although the wave-and-spike complexes were rather more prominent during treatment. In 4 patients primidone was discontinued at the end of a 6-month period of complete control; in 3 the fits did not recur, but one relapsed.

As regards side-effects, 3 patients developed a mild morbilliform rash during the first week of treatment, which disappeared in a few days. The blood count was determined and the urine examined as a routine in all cases, but no abnormality was found. During the first 48 hours of treatment 8 children vomited and 4 had abdominal pain, these reactions being severe enough for one patient to be admitted to hospital; 2 other patients became unduly drowsy. When, however, the first dose was given in the evening there was a reduction in the incidence of these symptoms. In one case a dose of only 0·125 g. led to acute toxic symptoms—abdominal discomfort, nausea, vomiting, ataxia, drowsiness, and slurred speech—which ceased when the drug was withdrawn; when administration of primidone was resumed there was no immediate reaction, but it had to be discontinued at a dosage of 0·75 g. daily because it failed to control the epilepsy and there was recurrent abdominal pain. A skin rash developed in 2 patients after 6 weeks' treatment, but in both it faded although the drug was not withdrawn. The earliest signs of over-dosage were ataxia, slurring of speech, and an unusual degree of talkativeness with loss of self-control. These symptoms quickly subsided with a reduction in the dose of primidone. *N. S. Alcock*

1742. **Primidone in the Treatment of Non-idiopathic Epilepsy**

P. W. NATHAN. *Lancet* [*Lancet*] **1**, 21–22, Jan. 2, 1954. 2 refs.

Primidone was tried at the National Hospital, Queen Square, London, in the treatment of 21 patients suffering from epilepsy due to organic disease of the brain, including congenital hemiplegia, porencephaly, cerebral neoplasm, cerebral abscess, and cortical atrophy. None of the patients had petit-mal epilepsy. Most of them were having several fits a day, none fewer than two a week, for which they were receiving phenobarbitone and phenytoin sodium without benefit. The routine dose of primidone was 0·5 g. three times a day.

Of the 21 patients, 9 were improved, 10 were no better, and 2 were worse. In the patients who improved there was a marked initial reduction in the number of attacks, although this was not consistently maintained; in none of them, however, were the attacks "even a quarter" as frequent as they were before treatment with primidone. The initial period of freedom from attacks ranged from 14 days to 16 months.

Toxic symptoms were sleepiness and ataxia; all the patients complained of sleepiness during the first week, when they were still receiving other anticonvulsant drugs, but when primidone was given alone this reaction ceased. One patient was ataxic on the routine dose of 1·5 g. a day, and 2 others were ataxic on 2 g. a day but not on 1·5 g. Another patient receiving 1·5 g. a day had ataxia and urticaria and complained of a sense of detachment and irresponsibility; these toxic manifestations cleared up when promethazine was given in addition to primidone, and did not recur when promethazine was withdrawn. Examination of the blood showed no abnormality. *N. S. Alcock*

1743. **The Use of "Mysoline" in the Treatment of Epilepsy**

P. J. DOYLE and S. LIVINGSTON. *Journal of Pediatrics* [*J. Pediat.*] **43**, 413–416, Oct., 1953. 1 ref.

It has been found that "mysoline" (primidone) protects animals against induced convulsions. The first clinical investigation of the value of the drug was that of Handley and Stewart (*Lancet*, 1952, **1**, 742; *Abstracts of World Medicine*, 1952, **12**, 166) in grand-mal epilepsy. Primidone was tried at Johns Hopkins Hospital, Baltimore, in the treatment of 100 epileptic patients, mostly children, with varying types of seizure as follows: grand mal, 51; petit mal (transient loss of consciousness with 3-per-second spike-and-wave forms in the EEG), 9; psychomotor seizures, 5; minor motor attacks (akinetic or myoclonic, of momentary duration), 11; and mixed epilepsy, 24. Epilepsy was regarded as idiopathic in 64 and secondary to organic disease in 36.

The results showed clearly that primidone is generally effective only against grand-mal epilepsy. The dosage employed was 125 mg. three times a day, rising to a maximum of 250 mg. 4 times a day, in patients under 6 years of age; in patients over 6 years the initial dose was 250 mg. twice a day, rising to 500 mg. 3 times a day. In 30 of the 51 patients suffering from major motor epilepsy the attacks were completely controlled, although in 26 the attacks had proved refractory to other anticonvulsant drugs; 8 patients were "markedly improved", 3 were "improved", and 10 failed to respond. In all the other groups combined the results were: controlled 0, "markedly improved" 12, and "improved" 10, with 27 failures. No serious side-effects were noted. Transient drowsiness was the most prominent reaction, but only in 4 cases was it sufficiently severe to cause discontinuance of the drug. Minor disorders of equilibrium were noted in 10 patients, but in all cases these disappeared without the dosage being altered. *Donald McDonald*

1744. **Indications for and Results of Cortical Excision in Temporal Epilepsy.** (Indications et résultats de l'excision corticale dans l'épilepsie temporale. (D'après 20 cas opérés))

D. PETIT-DUTAILLIS, J. CHRISTOPHE, B. PERTUISET, and C. DREYFUS-BRISAC. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **29**, 3838–3847, Dec. 2, 1953. 9 figs., 30 refs.

The 20 cases of temporal epilepsy here described were selected from among 38 cases of epilepsy not associated with a cerebral tumour operated on by the authors in the last 2½ years. The diagnosis of temporal epilepsy

was based principally on the symptomatology, electroencephalography being used to provide confirmatory evidence and to help in location as to laterality. Of the 20 patients, 14 underwent excision of the right temporal lobe, 5 of the left temporal lobe, and one of both lobes. The types of epileptic crisis seen were most commonly olfactory or gustatory, but one case of auditory hallucination and one of visual hallucination were noted. Aphasic attacks were observed in cases involving the left temporal lobe, and fits with gyratory or adversive movements were also of value in location. Peculiar visceral sensations were common and interruption of consciousness as in petit mal was frequent, but unconsciousness with falling was rare.

The extent of the surgical excision depended on the type of the epilepsy, but the results seemed best following fairly extensive removal, and in consequence were better in patients with right-sided disease as in them ablation was not limited by fear of encroaching on the speech areas. In cases with olfactory crises it was found necessary to remove the uncus, in spite of the doubt expressed by other workers regarding its connexion with the olfactory tract in the higher mammals. Regular 6-monthly follow-up examinations of the first 16 patients operated on showed an excellent result in 9 (56%), partial improvement in 2, and no change in 5. The other 4 patients have been operated on only in the last 6 months. There were no operative deaths. *Donald McDonald*

1745. **Bromides in the Treatment of Epilepsy in Children**
S. Livingston and P. H. Pearson. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **86**, 717–720, Dec., 1953. 11 refs.

Although bromides are not now extensively used in the treatment of epilepsy they are still considered to be of value at the Epilepsy Clinic of the Johns Hopkins Hospital, Baltimore, and in this paper the authors report the results obtained in 196 epileptic children, all of whom had severe organic brain lesions. A mixture containing equal parts of sodium, potassium, and ammonium bromide was given in a daily dosage of 0·6 g. to 1·8 g. to children under 6 years and 0·9 g. to 3 g. to children over that age. In 61 patients the fits were controlled, while in 54 others their frequency was greatly reduced. Of these 196 patients, 102 had been treated with the newer anticonvulsant drugs without success; with bromide therapy the fits were controlled in 28 and the incidence reduced in 26. Untoward drug reactions were rare, and the authors consider that bromides still have a place in the treatment of epilepsy in children.

*Winston Turner*

## SPINAL CORD

1746. **Spinal Epidural Abscess**
A. Hulme and N. M. Dott. *British Medical Journal* [*Brit. Med. J.*] **1**, 64–68, Jan. 9, 1954. 9 refs.

It is pointed out that although spinal epidural suppuration is a well-recognized clinical entity, it has received little attention in British literature. The authors therefore review their findings in 25 cases treated at the Edinburgh Royal Infirmary and the Bristol Neurosurgical Centre, and describe 10 in detail.

In most cases the causative organism is *Staphylococcus aureus*. The clinical features are back pain, root pains, motor and sensory loss, and sphincter disturbances, leading progressively to complete paraplegia. The onset is often fairly rapid, but in the chronic type of infection the course may be prolonged, extending over months or even years. The presence of pyrexia, leucocytosis, and headache, together with a positive blood culture, helps to establish the diagnosis, which is confirmed by evidence of spinal block; in some cases myelography is necessary to determine the level of the lesion. Once the diagnosis is established operation should be performed to release pus and decompress the theca and its contents, appropriate antibiotic therapy being given locally and systemically. If treatment is undertaken before there is gross impairment of conduction in the cord, results are good.

[Martin (*Brit. med. J.*, 1946, **2**, 688; *Abstracts of World Surgery*, 1947, **1**, 145) suggested that pyogenic osteomyelitis of the spine is commoner than is generally realized; he described 5 personal cases. Early recognition of the condition and appropriate chemotherapy and surgery are essential for satisfactory recovery.]

*Lambert Rogers*

1747. **Syringomyelia. A Clinicopathologic Study**
M. G. Netsky. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **70**, 741–777, Dec., 1953. 22 figs., 19 refs.

The clinical and pathological findings in 8 cases of syringomyelia seen at the Montefiore Hospital for Chronic Diseases, New York, are described. The author suggests that the cause of " true " syringomyelia is an anomaly of the intramedullary blood supply, and that when the patient reaches adult life, vascular insufficiency with occlusion leads to cavitation, gliosis, and fibrosis. He draws attention to the finding on clinical examination of loss of sense of vibration, although the position sense remains normal. He suggests that the pallaesthetic fibres may lie in the medial part of the lateral columns rather than in the posterior columns.

[Excellent illustrations accompany this paper.]

*J. W. Aldren Turner*

1748. **Embryological Stages in the Establishing of Myeloschisis with Spina Bifida**
B. M. Patten. *American Journal of Anatomy* [*Amer. J. Anat.*] **93**, 365–395, Nov., 1953. 23 figs., 33 refs.

At the University of Michigan Medical School, Ann Arbor, three human embryos showing different stages in the development of spina bifida with myeloschisis were serially sectioned in a plane at right angles to the defect; a full-term rabbit foetus showing a similar condition was also examined.

The youngest human specimen (crown–rump length 8 mm.) was normal except for the spinal defect in the lumbo-sacral region. The sections showed a greatly increased bulk of neural-plate tissue in the region of the defect; the only indication of the future vertebrae at this stage was a slight condensation of mesenchymal cells

about the notochord. In the next specimen (49 mm.) the vertebrae were well developed in cartilage and showed marked spina bifida. At the cephalic end of the lesion the neural tube was double, the two moieties lying side by side and each possessing a clear-cut ependymal lining. The third human embryo (160 mm.) showed in the region of the lesion a widely open neural plate with evidence of degenerative changes. The connective tissue underlying the neural plate contained many engorged blood vessels, and the subarachnoid space was also dilated. Ossification was beginning in the vertebrae, which showed marked lateral displacement of the neural arches. The rabbit foetus showed striking changes in the skin in the vicinity of the lesion, the epidermis being thin, the hair follicles and sebaceous glands poorly developed, and the dermis oedematous and with many engorged blood vessels. In the central part of the lesion the neural-plate tissue showed almost complete disintegration.

The possible causes of this condition are discussed in the light of experimental work, and the author suggests that the primary factor may be overgrowth of neural tissue interfering with closure of the neural tube rather than an " arrest of development ". *D. B. Moffat*

## DEMYELINATING DISEASES

1749. **Acute Disseminated Encephalomyelitis and Acute Disseminated Sclerosis. Results of Treatment with A.C.T.H.**

H. G. MILLER and J. L. GIBBONS. *British Medical Journal* [*Brit. med. J.*] **2**, 1345–1348, Dec. 19, 1953. 16 refs.

In 1953 one of the authors reported the results obtained with ACTH in the treatment of 7 cases of acute disseminated encephalomyelitis (*Brit. med. J.*, **1**, 177; *Abstracts of World Medicine*, **14**, 150). In the present paper the results obtained in 3 further cases and in 7 patients with acute exacerbations of disseminated sclerosis are described.

In the 10 cases of acute disseminated encephalomyelitis the results were, on the whole, " distinctly encouraging ". Encephalitis followed measles in 2 cases, varicella in 2, and respiratory infections in 3; it occurred in association with acute rheumatic fever in one case, after body chilling in one case, and apparently spontaneously (acute necrotic myelitis) in one. In 7 patients there was " marked improvement " during a 5-day course of ACTH, and in 5 of these " quite unequivocal clinical improvement " within 12 hours of the first injection. In 2 cases of subacute necrotic myelitis and acute measles encephalitis respectively, treatment was a " complete failure ". The authors [rightly] point out that in these conditions there is a tendency to spontaneous recovery, which is often rapid, and they cannot yet be certain that the course of the illness was in fact influenced by administration of ACTH; nevertheless they regard the evidence as suggestive.

In contrast the results of ACTH therapy in 7 cases of acute exacerbation of disseminated sclerosis (8 episodes) were " profoundly disappointing ".

The authors consider that the results may be interpreted in one of two ways: " either acute disseminated encephalomyelitis responds to ACTH and disseminated sclerosis does not, or neither disease is influenced by the treatment and the differences observed are inherent in the natural history of the two syndromes ". Although the second interpretation is considered to be the less likely one, " it cannot be doubted that the two conditions are distinct, although differentiation may be difficult in the acute stage ". *J. MacD. Holmes*

## MYASTHENIA GRAVIS

1750. **Sex and Age in Myasthenia Gravis as Critical Factors in Incidence and Remission**

R. S. SCHWAB and C. C. LELAND. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **153**, 1270–1273, Dec. 5, 1953. 3 figs., 4 refs.

The progress of 78 patients with myasthenia gravis treated by thymectomy at the Massachusetts General Hospital, Boston, is analysed and compared with that of a control group of patients not so treated, selected from a total of 250 and matched with the former group in respect of sex distribution, age of onset (within 5 years), severity of the disease, and presence or absence of thymoma.

Those patients, of all ages and both sexes, in whom a thymoma was demonstrable showed no evidence of improvement in their myasthenia after the operation. Similarly, thymectomy appeared to be contraindicated in males in whom the onset of the disease was after the age of 30. In females without thymomata, however, thymectomy appeared to be definitely beneficial. Unquestionable improvement occurred in 63% of all the females (53) who were subjected to thymectomy and in 34% of the female control subjects. The mortality was 15% for the former group, including operative deaths, and 28% for the latter. More data indicate that the disease is twice as common in young females as in young males and twice as common in older males as it is in females.

In view of this difference in response to operation between females and males, the distribution by decades of the onset of the disease was determined for the two sexes in a total of 367 cases in which accurate information was available. This showed that whereas myasthenic symptoms first developed before the age of 31 in 62% of the 202 females, the corresponding proportion of the 167 males was only 27%. For females the modal age of onset was 21 to 25 years (in 21%), whereas for males the mode was 61 and over (in 30%). The significance of this difference in age of onset is at once apparent in the various series of cases treated by thymectomy reported in the literature, in all of which there are two or three times as many females as males. This would be the obvious result of some selection of the surgical cases, since the most suitable subject for a serious operation such as thymectomy would be the younger patient.

*J. MacD. Holmes*

# Psychiatry

1751. **Autonomic Responses in Differential Diagnosis of Organic and Psychogenic Psychoses**
W. G. Reese, R. Doss, and W. H. Gantt. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **70**, 778–793, Dec., 1953. 8 figs., 18 refs.

Although a vast amount of material has accumulated since Pavlov's day regarding the conditioned reflex in animals, mainly dogs, little seems to have been published in regard to such studies on human beings. At the Veterans Administration Hospital, Perry Point, Maryland, the authors have made attempts to condition 8 normal subjects and 6 patients with moderate to severe degrees of dementia. The unconditioned stimulus was an electric shock to the hand, and the conditioning stimulus was a coloured electric light, different colours being used as negative and positive stimuli. The heart rate, amount of chest movement, skin resistance, and spontaneous and integrated hand movements were recorded by means of a Darrow photopolygraph.

All the subjects responded to the unconditioned stimulus, but the normal subjects showed a more marked inhibition of avoidance movements. These subjects also all developed motor conditioned responses with psychogalvanic changes, while all the patients failed to develop either. In neither group was the heart rate significantly affected. The authors conclude that discriminative conditioned responses are not elicited in patients with organic psychoses.

[In spite of the title of this paper, no cases of " psychogenic psychoses " were, oddly enough, included in the study.] *L. G. Kiloh*

1752. **A Contribution to the Study of Homeostasis in Schizophrenia and Other Psychoses.** (Contribution à l'étude de l'homéostasie dans la schizophrénie et les autres psychoses)
J. Delay, B. Lainé, H. Azima, and J. Puech. *Encéphale* [*Encéphale*] **42**, 385–406, 1953. 1 fig., bibliography.

The authors briefly review the literature on homeostasis in schizophrenia, with particular reference to the claim that homeostasis is disturbed in this syndrome. They have submitted this hypothesis to an experimental test by comparing the variations in blood levels of sodium, chloride, and potassium and in the alkali reserve and *p*H of the blood before, during, and after stress (electric convulsion) in 11 schizophrenics and 7 other psychotic patients suffering from melancholia, paranoia, or hypomania. From repeated estimations of these values, curves were drawn to show the mode of their return from post-stress levels to the levels existing before the stress.

The results show that the homeostatic mechanisms governing the acid–base equilibrium were identical in the schizophrenics and the patients with other psychoses, and also that there was no statistically significant difference in the values obtained from different individuals or from the same individual at different times. The variability of the successive phases of the curve of restitution was also almost identical. While stressing that they have no data for normal (non-psychotic) subjects with which to compare their curves, the authors conclude that the hypothesis of a disturbance of homeostasis in schizophrenia must be abandoned.

*J. B. Stanton*

1753. **Isoniazid in Treatment of the Chronic Schizophrenic Patient**
I. F. Bennett, D. Cohen, and E. Starer. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **71**, 54–65, Jan., 1954. 36 refs.

Isoniazid was given at the Veterans Administration Hospital, Coatesville, Pennsylvania, to 30 patients suffering from chronic schizophrenia, 30 similar patients serving as controls. Both groups were in the same ward and contained an equal number of patients with each sub-type of schizophrenia. The mean age of the treated patients was 38 years and of the controls 35 years; the mean duration of illness was 14 years in the treated group and 10 years in the control group. Most of the patients in the two groups had received insulin, with or without electric shock therapy. Of the 30 treated patients, 15 received 50 mg. and 15 received 100 mg. of isoniazid three times a day, the control group receiving a placebo. The behaviour of all 60 patients was assessed by three different observers.

Laboratory, clinical, and psychiatric examinations showed no significant difference between the treated and the control groups, nor was there any difference in behaviour. No permanent changes were observed in liver function or in the eosinophil count. Electroencephalography was possible in only 9 of the treated patients, and comparison of the tracings obtained before and after treatment revealed no change.

Side-effects included hyperreflexia in 5 and erythema multiforme in one of the patients receiving isoniazid.

*G. de M. Rudolf*

1754. **Prognostic Factors in Electric Convulsive Therapy**
R. F. Hobson. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **16**, 275–281, Nov., 1953. 24 refs.

In this paper the author describes an attempt made at the Maudsley Hospital, London, to predict the prognosis in 127 cases subjected to electric convulsion therapy by a statistical analysis of their clinical features, and thus to obtain some guidance in the selection of cases likely to benefit from this procedure. The group included a high proportion of patients with " uncommon features ", nearly all were depressed, and there was a high incidence

of neurotic traits. In each case the presence or absence of each of 121 clinical items was recorded. After treatment the patients were classified into those showing considerable or complete recovery, and those in whom there was little or no improvement. The relative frequency of the occurrence of the various clinical features in each of these two groups was evaluated by the phi-coefficient method.

Features shown to be favourable were: sudden onset, good insight, obsessional personality, an attitude of self-reproach, and short duration of the illness. Those shown to be unfavourable included hypochondriasis, depersonalization, emotional lability, neurotic traits, hysterical attitude to symptoms, intelligence above average, and a fluctuating course of the illness. The association of an obsessional personality with good insight was particularly favourable. Prediction of the outcome of treatment based on these criteria proved successful in 79% of cases. A list and definitions of some of the clinical criteria are given. *L. G. Kiloh*

1755. **Intensified Electroconvulsant Therapy. Review of Five Years' Experience**
R. J. Russell, L. G. M. Page, and R. L. Jillett. *Lancet* [*Lancet*] **2**, 1177–1179, Dec. 5, 1953. 1 ref.

Intensified electric convulsion therapy (E.C.T.) consists in administration of a series of stimuli at 150 volts, each lasting one second, with half-second intervals; 8 to 15 stimuli constitute one treatment, which is usually given daily. The fit is smooth, and is shorter and safer than that produced by the usual method of induction, the clonic phase being eliminated.

At the Three Counties Hospital, Arlesley, Bedfordshire, this method was employed in a total of 3,500 cases over a recent 5-year period. Patients with depressive psychoses required 2 to 7 treatments; all types responded equally well, and many were treated as out-patients. The average number of treatments needed in cases of puerperal psychosis was 5·5; all 54 patients were discharged from hospital, though 2 relapsed. In schizophrenia the results were at least as good as those obtained with insulin shock therapy. The method proved particularly valuable in the disturbed excited type of patient with chronic psychosis.

Cerebral stimulation was applied after intensified E.C.T. in 43 patients with depressive psychosis. It appeared to shorten the period of post-treatment confusion and to reduce tension, but the efficacy of E.C.T. was a little impaired and an extra treatment was usually required. *L. G. Kiloh*

1756. **Observations on 36 Patients with General Paresis Treated with Penicillin–Malaria and Penicillin Alone**
W. M. Cohn. *Psychiatric Quarterly* [*Psychiat. Quart.*] **27**, 637–649, Oct., 1953. 18 refs.

Of a series of 36 syphilitic patients with general paresis treated at Hudson River State Hospital, New York, between 1949 and 1951, 18 were treated with a total dose of 8,000,000 units of penicillin, given over 20 days, and 50 or more hours of malaria fever (temperature 103° F. (39·4° C)), the other 18 patients being given 8,000,000 units of penicillin alone. The cell count and protein level in the cerebrospinal fluid were the main factors determining the type and extent of treatment.

Clinical improvement was obtained in 11 patients (61%) treated with penicillin and malaria, and in 5 (27%) of those treated with penicillin alone. Among the former, 7 (38·8%) were well enough to be discharged, but among the latter only 3 (16·6%) reached this stage; 16 patients given combined treatment and 13 given penicillin alone showed serological improvement 6 months to 3 years after termination of treatment. Thus better results were obtained with penicillin–malaria therapy, but the lower average age of this group, the shorter duration of symptoms before admission to hospital, and the small numbers in the series tend to lessen the significance of the difference which, in the author's view, is not sufficiently great to justify the risks and trouble entailed in giving the combined treatment. *Richard de Alarcón*

1757. **Personality Factors in Adult Atopic Eczema**
J. T. McLaughlin, R. J. Shoemaker, and W. B. Guy. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **68**, 506–516, Nov., 1953. 2 figs., 10 refs.

The authors describe a study carried out at the University of Pittsburgh School of Medicine on 9 male and 21 female patients, ranging in age from 14 to 42, with atopic eczema. It consisted mainly of psychiatric interviews and appraisal of the social situation of the patient with, in 28 cases, an interview with the patient's spouse, mother, or sibling.

Four of the patients had mental illness bordering upon psychosis, and the other 26 showed some personality disorder of varying degree. There were a number of striking similarities of attitude and behaviour in the group—for example, all were guarded, reticent, tense, and passively immobile; all denied experiencing strong feelings of love or hostility; furious scratching and vivid flushing, in patients of both sexes, were the usual accompaniment of an otherwise unemotional discussion of disturbing topics; open anger or resentment at interview was rare, but when anger was expressed, this was often followed by a reduction in scratching.

A more detailed description of personality features in male and in female patients is given. The "eczema personality" is briefly outlined as follows: great passivity, excessive concern over acceptance by others, deep but distrustful dependence upon a parental figure, and inhibition of healthy aggressiveness. While more assertive people take action to meet the stress situation, these patients itch and scratch in fuming inactivity. The personality features described are found in other psychosomatic disorders.

[This study follows the current pattern of the North American school in discovering the same personality features in all their cases of eczema. While everyone knows that eczema behaves as a stress disorder in many people, it is hard to believe that the pathogenetic mechanism is identical in every patient, and quite impossible to suppose that this mechanism is present in all the victims of every stress disorder.] *Desmond O'Neill*

# Dermatology

1758. **Reticular Lesions in Eosinophilic Granuloma.** (Lésions réticulaires dans le granulome éosinophilique)
A. NANTA, A. BAZEX, and A. DUPRÉ. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph.* (*Paris*)] **80**, 569–573, Nov.–Dec., 1953. 2 figs.

In 2 cases of eosinophilic granuloma (one of the skull invading the scalp and one hypodermal) a network of hyalinized reticulin was seen outside and inside the (hyalinized) membrane of fat vesicles. It is suggested that this reticulin network may play an active part in physiological or pathological lipid metabolism, changes in which cause not only cellular alteration but also, at times, more or less autonomous interstitial reticulin changes. *James Marshall*

1759. **Quinacrine Hydrochloride (Atabrine) in the Treatment of Lupus Erythematosus**
R. R. KIERLAND, L. A. BRUNSTING, and P. A. O'LEARY. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **68**, 651–663, Dec., 1953. 4 figs., 14 refs.

1760. **Acute Febrile Malignant Pemphigus. Case Report and Discussion of Classification.** (Pemphigus aigu fébrile grave. Relation d'un cas. Discussion sur la position nosologique de cette affection)
X. VILANOVA and J. PINOL AGUADÉ. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph.* (*Paris*)] **80**, 574–596, Nov.–Dec., 1953. 9 figs., bibliography.

The authors describe a fatal case of acute pemphigus treated at the University Dermato-syphiligraphic Clinic, Barcelona, the clinical features of which resembled in all respects those described by Nodet and by Brocq under the name of "acute febrile malignant pemphigus". A farm labourer aged 17 developed a whitlow and, soon afterwards, typical impetigo of the face and neck. A month later he suddenly became gravely ill, and large bullae, arising from an erythematous base, appeared and covered the entire surface of the skin. Sulphonamides and penicillin caused a spectacular improvement in the skin condition, but a week later he developed repeated convulsions, due probably to hypertensive encephalopathy, and died in 8 hours.

On microscopical examination of the skin post mortem the line of cleavage in the bullae was shown to lie between the dermis and the epidermis, as in dermatitis herpetiformis; the only point of distinction from the latter disease was that the elevated epidermis showed a polynuclear exocytosis. Negligible changes were found in the other organs, apart from oedema and hyperaemia of the meninges and cerebrum.

The differential diagnosis from other bullous diseases is discussed in detail. The authors are in complete disagreement, on histological grounds, with the opinion of Lever that this form of pemphigus is identical with the Stevens–Johnson syndrome; and they distinguish it from the septicaemias with bullous lesions. The literature on pathogenesis is reviewed, and the evidence in favour of considering acute febrile malignant pemphigus as a bacterial allergid is discussed. *James Marshall*

1761. **Hyperkeratotic Genodermatoses of the Bullous Type.** (Les génodermatoses hyperkératosiques de type bulleux)
S. LAPIÈRE. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph.* (*Paris*)] **80**, 597–614, Nov.–Dec., 1953. 6 figs., 24 refs.

A number of cases of hyperkeratotic genodermatoses of bullous type are described, together with the histological findings, and a classification of these conditions is suggested.

In a case of bullous ichthyosiform erythrodermia the essential histological lesions were *altération cavitaire*, partial acantholysis, and the formation of dyskeratotic bodies and little irregular spaces in the upper layers of the stratum mucosum and the stratum granulosum, the rupture of the thin walls of these spaces giving rise to superficial bullae. Four cases of bullous Darier's disease in three generations of a family are also described; in one of these the subject was stillborn, and in another the patient died at 3 weeks of age.

The author separates the ichthyoses into two clinically and histologically distinct groups, bullous and non-bullous. The bullous variety of Darier's disease presents no real histological differences from the dry type; and familial benign pemphigus may well be related to Darier's disease. *James Marshall*

1762. **Atopic Dermatitis. A Study of Its Natural Course and of Wool as a Dominant Allergic Factor**
E. D. OSBORNE and P. F. MURRAY. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **68**, 619–626, Dec., 1953. 6 refs.

The natural history of atopic dermatitis was studied at the University of Buffalo School of Medicine from the records of more than 2,500 patients from the age of 2 weeks to late adult life. It was found that in 30 to 40% of cases of dermatitis in infants under 1 year the condition was due to external sources of primary irritation, especially alkalis and external medicaments, and that it cleared up with simple soothing remedies. In 75% of children up to 2 years of age the dermatitis started in the cold months, September to March, and the authors regard this increased incidence as due primarily to exposure to wool, both by contact and by inhalation. They conclude that contact with wool fibre is the dominant allergenic factor in about two-thirds of the cases in which atopic dermatitis is exacerbated during the cold months and clears up in the warm months. Woollen caps, collars, coats, mufflers, sweaters, and mittens, also woollen rugs,

carpets, blankets, and furniture coverings are considered to be responsible for dermatitis at certain sites, principally on the cheeks, submental area and sides of the neck, wrists, and hands. If exposure to wool and inhalation of wool fibre continue, a generalized hypersensitivity to wool protein develops in a high proportion of cases, which is manifested by the characteristic flexural dermatitis of children and adults. The skin of most subjects with seasonal atopic dermatitis begins to itch and burn when the amount of wool fibre in the house dust exceeds 2%.

Discussing the significance of white dermographism in atopic dermatitis the authors conclude that the nature of the protein molecule of wool is responsible for the characteristic vasoconstriction, as well as for disturbances in the nervous, gastrointestinal, and cardiovascular systems which are commonly seen in these patients.

*E. W. Prosser Thomas*

1763. **Topical Neomycin–Bacitracin Therapy in Pyogenic Skin Infections.** [In English]
M. GADE, B. KORNER, and B. SYLVEST. *Acta dermato-venereologica* [*Acta derm.-venereol.* (*Stockh.*)] **33**, 476–487, 1953. 29 refs.

At the Rudolph Bergh Hospital, Copenhagen, the authors have used for topical application an ointment containing 5 mg. of neomycin and 250 units of bacitracin per gramme of a base consisting of 10% of lanolin in soft paraffin in the treatment of 74 in-patients suffering from various types of infected skin lesion. In those subjected to bacteriological examination a wide range of organisms were identified, of which by far the most common were various strains of staphylococci; all the strains were sensitive to this combination of antibiotics. The results of treatment were judged to be " excellent " in 38 cases, " good " in 10, " fair " in 6, " transitory " in 9, and " insignificant " in 2; in 5 cases there was no change, and in 4 in which there was aggravation of the condition this was shown to be due to the base. Sensitization did not occur.

*E. Lipman Cohen*

1764. **Erythromycin in Local Treatment of Cutaneous Bacterial Infections**
C. S. LIVINGOOD, E. S. HEAD, E. A. JOHNSON, and S. NILASENA. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **153**, 1266–1270, Dec. 5, 1953. 4 figs., 13 refs.

The effect of topical application of erythromycin in 184 cases of cutaneous bacterial infection of various types is described in this paper from the University of Texas School of Medicine, Galveston. For most of the patients an ointment containing 0·5% of erythromycin was used; a few were treated with a 1% ointment, or an ointment containing both neomycin and erythromycin, or an aqueous solution of erythromycin. Good results were obtained in cases of impetigo, ecthyma, furunculosis, and paronychia (one case only). As expected, the results in cases of secondary cutaneous bacterial infection were less satisfactory. In 3 patients there was an apparent sensitivity to erythromycin, as shown by exacerbations of existing skin lesions; 2 other patients reacted similarly to the ointment containing neomycin and erythromycin. The authors believe that erythromycin is slightly more irritating to denuded and eczematized skin than neomycin, bacitracin, aureomycin, or oxytetracycline.

Results of tests *in vitro* for 60 strains of haemolytic *Staphylococcus aureus* and 49 strains of β-haemolytic streptococci showed that the antibiotics which were effective against both groups of organisms were erythromycin, neomycin and bacitracin combined, and aureomycin, in that order of efficacy.

The authors conclude that while erythromycin promises to be useful in the treatment of skin infections, the possible development of resistant strains of staphylococci and streptococci and of side-effects must be borne in mind.

*G. W. Csonka*

1765. **Asterol Treatment of Superficial Dermatomycoses due to *T. mentagrophytes* and *T. purpureum***
E. EDELSON and A. H. HASKIN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **68**, 627–630, Dec., 1953. 5 refs.

At Newark Board of Health Clinics, New Jersey, " asterol " dihydrochloride (2-dimethylamino-6-[*beta*-diethylaminoethoxyl]-benzothiazole) in the form of ointment, tincture, and dusting powder was used in the treatment of 97 cases of mycosis of the feet, glabrous skin, and onychomycosis; the causative fungus was *Trichophyton mentagrophytes* in 39 cases and *T. rubrum* in 58. The results in the former group were " gratifying ", but in *T. rubrum* infections the cure rate was not higher than that achieved with other fungicides.

[Every dermatologist will agree that " it is very difficult to determine the comparative merits of various agents recommended for the treatment of dermatomycoses ".]

*E. W. Prosser Thomas*

1766. **Neomycin Lotion in Treatment of Cutaneous Bacterial Infections**
M. A. FORBES. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **68**, 631–634, Dec., 1953. 20 refs.

It is pointed out that neomycin is the only broad-spectrum antibiotic at present available which is stable in an aqueous solution for an indefinite period. Because of this, a lotion of neomycin can be prepared which is convenient to apply in skin infections and is preferable, in some cases, to wet dressings or an ointment. Neomycin lotion was used at the University of Texas School of Medicine, Austin, in the treatment of 126 patients with cutaneous bacterial infections. The lesions were cleansed with soap and water and the lotion applied twice a day. Of the 126, 109 responded satisfactorily within 7 days. Impetigo, folliculitis, and ecthyma cleared up more rapidly than impetiginized eczematous dermatitis and otitis externa. In none of the cases was primary irritation or sensitization noted, but one patient with infected eczematous dermatitis of the toes developed localized moniliasis, which, however, cleared up a few days after application of the lotion was stopped.

*E. W. Prosser Thomas*

# Paediatrics

## NEONATAL DISORDERS

1767. **The Results of a National Inquiry into the Growth of Premature Children from Birth to 4 years**
J. W. B. DOUGLAS and C. MOGFORD. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **28**, 436–445, Dec., 1953. 2 figs., 13 refs.

This paper describes the growth of a national sample of premature children who have been followed up from birth to 4 years and who, throughout this period, have been contrasted with a closely matched group of controls.

On the average the premature children have not reduced their weight handicap between birth and 4 years, and have not reduced their height handicap between 2 and 4 years. By 4 years of age, 36% of premature children have caught up with or surpassed their controls in weight and 44% in height. There is a tendency for the smallest premature children at birth to be the most successful in eliminating their initial handicaps. There is no statistically satisfactory evidence that premature children resulting from the shorter gestations or from complicated pregnancies differ in their rate of growth from the rest of the premature sample.

The mothers of premature children are on the average shorter and lighter than the mothers of the controls, and the premature children who are furthest behind their controls in weight or height tend also to be the ones whose mothers are furthest behind the mothers of the controls in these measurements. The mothers of the premature children, who by 4 years have eliminated their initial weight or height handicaps, are as tall and as heavy as the mothers of the matched controls. In contrast the mothers of the children who are still lagging behind at this age are significantly smaller and lighter than the mothers of the controls.

Premature children yield more than their share of all children who are stunted or underweight. But removal of all premature children would make only a relatively small reduction in the numbers of children of this type in the whole population. There is no satisfactory evidence that the premature children who come from the relatively well-to-do families are any more successful in reducing their physical handicaps than those from poorer families.—[Authors' summary.]

1768. **The Developing Fundus Oculi of the Premature Infant and its Relationship to Retrolental Fibroplasia**
M. C. FLETCHER. *Journal of Pediatrics* [*J. Pediat.*] **43**, 499–523, Nov., 1953. 10 figs., 13 refs.

The author studied the development of the eyes of 320 premature infants from birth to the age of 6 months at Jefferson Davis Hospital, Houston, Texas. Most of the infants weighed less than 1,700 g. at birth. The eyes were examined by direct ophthalmoscopy, a small lid retractor being used and atropine given as a mydriatic.

From his findings in these cases, the author concludes that about 50% of infants weighing less than 1,500 g., and nearly all infants weighing less than 1,250 g., are born with an immature fundus, which remains unchanged for several weeks and then rapidly matures. The immature features are an oval disk, small, scanty vessels, a vitreous haze, and a slate-coloured peripheral retina; hyaloid remnants and pupillary membranes are the rule. The eye may mature and remain normal, or after maturation it may go on to show the early hypervascular changes of retrolental fibroplasia, which may regress spontaneously or may progress to the more severe stages of the disease with varying degrees of visual impairment. The early hypervascular changes of retrolental fibroplasia are venous dilatation, tortuosity of the arteries, retinal haemorrhages, blurring of the disk margin, retinal oedema, and reappearance of the vitreous haze; iritis may occur and the tension is often raised. These changes may be followed by the development of opaque tissue at the periphery, retinal folding, detachment, retrolental tissue, and vitreous haemorrhage.

Of the 320 infants examined, 86 had retrolental fibroplasia; 38 of these developed massive retinal oedema with detachment and malignant haemorrhages. The incidence of the disease was significantly higher in white than in negro infants, and in males than in females. The smallest infants and those with the most immature fundi at birth appeared to be the most likely to develop retrolental fibroplasia.

The first appearance of the disease in Houston seemed to coincide with the establishment of a modern unit for the care of premature infants, with a resulting increase in the survival rate among very small babies. Evidence is also presented to show that small premature infants and infants with retrolental fibroplasia have a high and fluctuating myopia which may remain as a residual lesion. A number of possible pathogenic factors are discussed, but the author concludes that retrolental fibroplasia results from an as yet unknown factor affecting an immature eye when it is passing through a period of differentiation and maturation.

The paper is illustrated with 36 drawings of the fundus, some reproduced in colour. *J. Foley*

1769. **Oxygen Studies in Retrolental Fibroplasia. II. The Production of the Microscopic Changes of Retrolental Fibroplasia in Experimental Animals**
A. PATZ, A. EASTHAM, D. H. HIGGINBOTHAM, and T. KLEH. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **36**, 1511–1522, Nov., 1953. 7 figs., 7 refs.

An extensive study of the effect of oxygen on the eyes of young or immature animals was made at the Gallinger Municipal Hospital, Washington, D.C. Parturient opossums with young in the pouch were subjected to intermittent exposure to 70% oxygen, but because of the

susceptibility of the mothers to bronchopneumonia this experiment had to be abandoned; none of the young showed any changes in the eye or other organs. Groups of pregnant albino rats were then exposed for various periods to intermittent 90% oxygen, and other groups of pregnant rats were exposed intermittently to 100% oxygen at two atmospheres pressure; no ocular abnormalities were found amongst the foetuses or young.

When, however, rats within the first 18 hours of life were maintained in continuous 80% oxygen for 21 days, 12 of the 27 test animals showed ocular lesions in 17 eyes. The abnormalities were persistence and proliferation of the tunica vasculosa lentis, disorganization of the vitreous, and oedema of the retina. Three groups of newborn white mice similarly maintained continuously in 80% oxygen showed a correlation between the ocular changes and the length of exposure to oxygen. Common lesions were haemorrhage, persistence and proliferation of the tunica vasculosa lentis, vitreous degeneration, retinal oedema, and endothelial- or glial-cell nodules in the nerve-fibre layer. Similar ocular lesions were observed in all members of 4 litters of newborn kittens and in 2 litters of puppies reared in an atmosphere of 70% oxygen.

The authors conclude that high concentrations of oxygen alone may produce changes in the eyes of young animals resembling those of retrolental fibroplasia in the human infant, and that these injurious effects may be accentuated by rapid withdrawal of the oxygen. They urge rigid curtailment of the use of oxygen therapy for premature infants, and that when oxygen must be used, the amount should be prescribed by concentration rather than by rate of flow and frequent estimations of oxygen tension made.

[This paper should be read in full by all interested in the problem of retrolental fibroplasia.] *B. Ward*

1770. **Postmaturity—With Placental Dysfunction. Clinical Syndrome and Pathologic Findings**
S. H. CLIFFORD. *Journal of Pediatrics* [*J. Pediat.*] **44**, 1–13, Jan., 1954. 12 figs., 18 refs.

Postmaturity, defined as being due to prolongation of pregnancy to 300 days or more, is a danger to foetal and neonatal survival, as is well illustrated in this paper from the Boston Lying-in Hospital (Harvard Medical School) in which its effects on 37 infants in different stages of postmaturity are discussed. Placental dysfunction and loss of the protective vernix caseosa are regarded as the immediate causes of the clinical findings in these infants.

Three stages of postmaturity are described. (1) The first is characterized by the well-known " post-mature " skin, which is wrinkled and peeling in an infant who is long and thin and with the appearance of having recently lost weight; 13 of the author's cases were in this group; there were no deaths, but 4 infants required special care. (2) The second stage has the added feature of staining by meconium of the amniotic fluid, placental membranes, and umbilical cord; of 11 such infants, 4 died, 3 needed special paediatric care, and the remaining 4 were normal. (3) The third stage carries a high intra-uterine foetal mortality, but live-born infants show all the features of the other two stages as well as bright yellow staining of the skin and nails and a dirty yellow staining of the umbilical cord; among the 13 infants in this group there were 2 deaths, but as the author points out, the more seriously affected infants die in utero. The infants' weights and lengths, the estimated duration of postmaturity, and the age and parity of the mothers are recorded for the three groups.

*David Morris*

## CLINICAL PAEDIATRICS

1771. **Hemolytic Streptococcal Infection in Childhood**
L. A. RANTZ, M. MARONEY, and J. M. DI CAPRIO. *Pediatrics* [*Pediatrics*] **12**, 498–515, Nov., 1953. 9 refs.

A study was made of haemolytic streptococcal infection in the first 8 years of life among infants and children attending the out-patient clinics of Stanford University Hospitals, San Francisco, including a serial study of a group of babies from birth until the end of the fourth year. In the first 4 years of life the infection tended to be characterized in its most severe form by an insidious onset, low-grade fever or none at all, rhinorrhoea, a protracted course, and the frequent occurrence of suppurative complications. After the fourth year the disease pattern changed, more of the infections being characterized by an acute febrile onset, sore throat, exudative tonsillitis and pharyngitis, and occasionally a rash.

It is suggested that the change in pattern of clinical response to haemolytic streptococci is due to repeated infection causing an alteration in tissue reactivity, probably of immunological origin. *R. S. Illingworth*

1772. **Haemoptysis, Bronchiectasis, and Foreign Body in Lung**
B. LAURANCE. *British Medical Journal* [*Brit. med. J.*] **1**, 125–127, Jan. 16, 1954. 2 figs., 14 refs.

The cases of 3 children are reported from the Bristol Royal Hospital for Sick Children, in whom respiratory symptoms and physical signs were found after some delay to have been caused by inhaled foreign bodies. The first patient, a boy of 5, choked over a piece of " grass in seed ", and a week later had an attack of pneumonia leading to chronic suppuration and later to repeated haemoptysis. Bronchoscopy on 3 occasions showed only suppuration and mucosal congestion, and a year after onset lower lobectomy revealed a fusiform dilatation of a bronchus containing an ear of wild barley. In the other patients, 18 months and 2½ years old respectively, an acute respiratory infection was associated with and followed by evidence of lobar collapse; on bronchoscopy a vegetable foreign body was found and successfully removed, with subsequent complete recovery in each case.

The authors point out that vegetable matter, which is not opaque to *x* rays, may swell by imbibition and irritate the tracheo-bronchial mucosa, causing a cough with purulent sputum which may be streaked with blood from granulation tissue. In any case of persistent re-

spiratory disease in a child, therefore, a history of choking over any material should be carefully sought for and, if elicited, should lead to thorough investigation. Although lung abscess is rare in children, any form of chronic suppuration, especially of the right lung, should raise suspicion of the presence of a foreign body.

*A. W. Franklin*

1773. **The Infant with Stridor. A Follow-up Survey of 80 Cases**

J. APLEY. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **28**, 423–435, Dec., 1953. 9 figs., 16 refs.

Observations are recorded on 80 cases with stridor developing in early infancy. To determine the natural history of the condition progress was assessed clinically and by ancillary methods for periods up to several years. Attention was directed not only to the sequence of any changes in the larynx, but also to general physical and mental development.

Stridor occurred in 11 of 14 siblings in 5 families. In the whole series there was a male preponderance, in the ratio of 5 boys to 3 girls. The average birth weight of males was significantly higher than that of females with stridor, and of unselected infants of either sex. In 7 cases a congenital cardiac malformation was present, though in only one was it the cause of stridor. Three patients in the series were mongols; 16 others were mentally retarded. Feeding difficulties occurred in half the total number. Pulmonary complications were frequent. Chest deformities developed in many cases but were almost invariably transient. Eleven patients died, and in 10 necropsy was performed. Apart from 2 cases of meningo-myelocele and one of thyroid enlargement, death was invariably due to pulmonary infection.

In the largest group of cases stridor was produced by an anatomical anomaly which impaired the patency of the upper respiratory tract; in the majority of these the anomaly was epiglottic. In a second group stridor was considered to be due to dysfunction of the nervous system. In a third group stridor originated with an upper respiratory infection.

The mechanism of production of stridor in these groups is discussed, with particular reference to primary and secondary changes in the larynx. It is emphasized that in the investigation of infantile stridor it is essential to make early and repeated observations, not only of the larynx and respiratory tract, but of the patient as a whole.—[Author's summary.]

1774. **Acute Gastroenteritis. A Review of 518 Cases Treated at the Hospital for Sick Children during 1951 and 1952**

M. G. WOLFISH. *Journal of Pediatrics* [*J. Pediat.*] **43**, 675–686, Dec., 1953. 3 figs., 24 refs.

The author reviews 518 cases of acute gastroenteritis in infants under 2 years admitted to the Hospital for Sick Children, Toronto, between July, 1951, and December, 1952. The infants were from all social classes and income groups among the population. The incidence was highest at the age of 2 months; no significant seasonal incidence was noted. Of the first 300 infants only 11 were breast-fed for longer than 2 months, and only 2 were breast-fed at the time of onset of the illness. A proved enteric pathogen was recovered from the stool in only 23 cases (4·4%) in the whole series. Parenteral infection was found in 207 (40%) of the infants on admission, including 123 with upper respiratory infection and 46 with otitis media. In the remaining 288 patients (55·6%) no known aetiological agent was identified. The author states that bacteriological investigation did not include the isolation of viruses or identification of the serotypes *of Bacterium coli*.

The clinical features of dehydration in these patients are discussed, and methods of treatment are outlined. The author emphasizes the value of blood or plasma transfusion and intravenous infusion of fluids for treatment of the initial collapse, correction of water and salt depletion, and maintenance of fluid and mineral balance. In those dehydrated infants in whom the blood chemistry was studied there appeared to be no relationship between the serum potassium level, the clinical course, and the length of stay in hospital. Potassium replacement therapy was given to 40% of the infants in the series. Early frequent feeds of small quantities of clear fluid were well tolerated; the duration of vomiting and of diarrhoea was not shortened by withholding food by mouth for the first 24 hours. When feeding was resumed dilute milk was given, the author having found that relapse was more frequent among infants given full-strength feeds.

Antibiotic therapy was of value in the prevention and treatment of intercurrent infection, but did not affect the gastroenteritis or the length of hospital stay. In this series 17 patients died, a mortality of 3·3%; of these 17, 6 died within an hour of admission and received no treatment of any kind, the mortality among the treated patients thus being 2·1%. *M. MacGregor*

1775. **Acute Nephritis in Early Infancy.** (Les néphrites aiguës du nourrisson)

J. MARIE and P. SERINGE. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **29**, 3765–3775, Nov. 26, 1953. 5 refs.

In this review of 42 cases of acute nephritis in infants seen at the Hôpital Hérold, Paris, during the period 1944–8, to which the authors have added a few more recent cases, the main part of the paper is devoted to an attempt to identify ten different clinical forms of the disease, some of which are exemplified by brief case reports. These include, beside the well-recognized anuric, oedematous, albuminuric, haematuric, and anaemic types, a " hepato-renal " type (in which there are hepatomegaly, jaundice, purpura, and hypoprothrombinaemia), and an " eclamptic " type, comparable with hypertensive encephalopathy, but these last two types are rarely encountered. The aetiology is summarily discussed under four headings: infective, toxic, acute primary, and the type of nephritis associated with a toxic state of infants [which helps not at all in our understanding of this obscure disease. There is no review of the series from the point of view of age incidence, sex distribution, duration, or outcome, and there is no mention of any bacteriological studies.] *David Morris*

# Medical Genetics

1776. **Studies on the Heredity of the Human Blood Groups. I. The M–N Types.** [In English]
A. S. WIENER, N. DI DIEGO, and S. SOKOL. *Acta geneticae medicae et gemellologiae* [*Acta Genet. med. (Roma)*] **2**, 391–398, Sept., 1953. 16 refs.

The distribution of the MN types of blood agglutinogen in a series of 420 New York families with 645 children is recorded. The findings were in complete conformity with the theory of Landsteiner and Levine that these types are inherited through a pair of allelic genes.

The distribution of MN types was also determined among 954 professional blood donors, of whom 394 were tested for the S factor: the gene frequencies (M=0·5484, N=0·4414) agreed well with expectation. It is concluded that in skilled hands tests based on determination of the MN types are entirely reliable for medico-legal use. *George Discombe*

1777. **Studies on the Heredity of the Human Blood Groups. II. The A–B–O Groups.** [In English]
A. S. WIENER, E. B. GORDON, and L. COHEN. *Acta geneticae medicae et gemellologiae* [*Acta Genet. med. (Roma)*] **3**, 29–33, Jan., 1954. 1 ref.

The distribution of the ABO groups in a series of 426 New York families with 649 children is recorded. No cases were encountered which failed to conform to the multiple-allele theory of the heredity of the $A_1A_2BO$ blood groups, and the frequencies of these blood groups among the children showed satisfactory agreement with those expected on the basis of this theory. The tests for the sub-divisions of Group A are, however, thought to be insufficiently reliable for medico-legal use.
*George Discombe*

1778. **ABO Blood Groups and Human Fertility**
T. M. ALLAN. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **7**, 220–226, Oct., 1953. 30 refs.

An analysis was made by Waterhouse and Hogben in 1947 (*Brit. J. soc. Med.*, **1**, 1) of 12 family studies published between 1927 and 1944, their object being to elucidate the mode of inheritance of the ABO blood groups. The present author, carrying the analysis of the same series a stage farther, shows that when the mating classes in which the parents are of the same group are omitted from the sample, the descending order of fertility among fathers of the various groups is B, AB, O, and A, while among mothers it is precisely the reverse—A, O, AB, B. The fertility of Group-A husbands is always less than that of Group-B husbands with wives of the same group, whatever it may be, so that these differences in fertility cannot be attributed to maternal–foetal incompatibility. The author suggests that further studies are necessary to show whether these differences in fertility are more than a chance finding. *C. O. Carter*

1779. **The Sex Ratio in Convulsive Disorders with a Note on Single-sex Sibships**
C. OUNSTED. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **16**, 267–274, Nov., 1953. 19 refs.

Previous surveys of the relative sex-incidence of convulsive disorders in childhood have shown a preponderance of males ranging from 57 to 62%. In the present study, carried out at the Radcliffe Infirmary, Oxford, the author examined 200 consecutive propositi, aged between one day and 12 years, suffering from convulsive disorders (including all recognized convulsive syndromes and individual seizures) seen either as in-patients or in the out-patient department of the hospital or reported by ancillary medical services in Oxford. As clear a history as possible of the incidence of convulsions in sibs, parents, aunts, uncles, and grandparents was obtained by questioning of the patient's mother.

The percentage of males was as follows: among all propositi, 59%; among epileptic propositi, 57·9%; among all (277) sibs of propositi, 56·3%; among propositi and affected sibs, 57·3%; and among unaffected sibs, 57·6%. It thus appears that within families which manifest seizures, sex is not a significant aetiological factor. Nevertheless, the sex ratio of children who are affected (134 males to 100 females) considerably exceeds the normal sex ratio at birth (105 males to 100 females).

In the group with a positive family history (that is, a clear history of convulsive disorder in any one of the above-mentioned relatives) the sex ratio was 105·3 males per 100 females; but in the group with no family history of seizures it was 160·5 per 100. The incidence of convulsions was, however, almost exactly the same (55% of males and 56% of females) whether there was a positive family history or not. In the group with a negative family history, analysis of sibships showed a great excess of all-male sibships, but no excess of males among mixed sibships. In the group with a positive family history, however, the observed incidence of all-male, mixed, and all-female sibships tallied closely with expected values. Similar results were obtained for a second series of 137 propositi and their sibs.

It is concluded that in the families of children with convulsive disorders (including epilepsy) there is an association between a tendency for male single-sex sibships and the absence of seizures among the patient's close relatives; and also that although the ratio of males to females among affected children is greater than unity, there is no apparent difference in incidence of the disorder in the two sexes. The author adds: "The findings suggest that the use of a differential sex ratio to measure the aetiological weight of sex is a suspect procedure." *R. H. Cawley*

# Public Health

1780. **The Epidemiology and Prevention of Tuberculosis in Cornwall**
E. R. HARGREAVES. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **47**, 192–201, Oct., 1953. 3 figs., 4 refs.

The post-war mortality from tuberculosis in Cornwall, although below that for England and Wales, has been higher than in other south-western counties, owing mainly to the existence of a few "black spots" where the mortality was much higher than it was in the rest of the county.

The county Public Health Department has therefore carried out an investigation in the worst two areas, namely, the urban districts of St. Just in the farthest north-westerly corner of the county and Penryn, near Falmouth. The method consisted of investigation of the contacts of known cases of tuberculosis, and segregation and vaccination with B.C.G. of the negative contacts. School-children were subjected to a tuberculin survey, and a mass-radiography unit visited the areas for the screening of adults and tuberculin-positive children. The response to tuberculin testing in school-children was good, but less than half (44·5%) of the general population came forward for radiography. A very high incidence of active pulmonary tuberculosis was found in St. Just (7·9 cases per 1,000 of the population) by the mass radiography unit. Although disappointing in some respects, the investigation achieved much good work, particularly in the locating of dangerous sources of infection.

[The title of this paper is rather misleading, as the investigation was concerned with only some 8,000 out of Cornwall's total population of 340,000.]

*J. Lorber*

1781. **History of Poliomyelitis in Cornwall and Devon**
A. H. GALE and E. R. HARGREAVES. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **7**, 180–193, Oct., 1953. 6 figs., 10 refs.

1782. **An Epidemic of Conjunctivitis in Colorado. Associated with Pharyngitis, Muscle Pain, and Pyrexia**
T. A. COCKBURN. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **36**, 1534–1539, Nov., 1953. 1 fig.

In August and September, 1951, an epidemic of conjunctivitis occurred in the town of Greeley, Colorado (population 21,000), affecting 206 persons, of whom 58 were studied in detail by the author. Similar epidemics involving some thousands of cases were reported to have occurred in other towns in Missouri and Colorado in the same months of the previous year. The main features of the illness were an acute, non-purulent conjunctivitis—sometimes followed by a mild keratitis—vesicular pharyngitis, muscular pains, and pyrexia. Most of the patients were treated at home by the family physician in view of the relatively mild nature of the disease; several of the more severely ill patients were suspected in the early stages to be suffering from poliomyelitis. The spread of infection in the epidemic was known in some cases to be by direct transmission between members of affected families, but there was strong presumptive evidence that in many cases infection took place at the one, much-frequented, local swimming pool. No infective agent was discovered by laboratory studies. *R. Smith*

1783. **Work and Age: Statistical Considerations**
W. P. D. LOGAN. *British Medical Journal* [*Brit. med. J.*] **2**, 1190–1193, Nov. 28, 1953. 7 figs.

During the past century the proportion of the population of England and Wales of working age (15 to 64) has increased, reaching 67% in 1951, but this is probably the peak and by 1991 it is likely to have fallen to 63%. Whereas 100 years ago there were 8 children under 15 for every person over 64, there are now only 2, and by 1991 the numbers will be about equal. In 1841 the expectation of life of males at birth was 40 years; it is now 66. At the age of 60, however, the expectation of life has increased only from 14 to 15 years (18 for females) in the same period. None the less, the age structure of the older part of the male population has not remained static; the ratio of the number of men over 75 to the number aged 60–64, which was 1:2 in 1841 and 1901, was 2:3 in 1951, and the two groups may be expected to be equal by 1991.

The occupational distribution of the elderly, as indicated by the 1% sampling of the 1951 census returns, shows that 87% of men in the age group 60–64 were still working full time. This proportion fell to 48% for the 65–69 group, and to 20% for men of 70 and over. As might be expected, employed operatives retire first, managers and the self-employed last. By the age of 70, 96% of rail transport workers (compared with 77% of all workers) were retired, but only 63% of those described as directors and managers, and only 59% of those engaged in agriculture. Farmers and farm-workers also continue to show, according to the 1951 returns, a low occupational mortality, the rate being 69% and 74% respectively of that for the male population as a whole at ages 60–64 compared with 98% for clerical workers, 108% for transport workers, and 187% for certain categories of mine-workers.

Some information concerning the frequency of absence from work through illness among the elderly can be obtained from the results of the monthly Survey of Sickness carried out in 1944–51. Surprisingly, in an average month in 1950, the average number of days of incapacity for men over 65 was little more than for those of working age, 89·1 and 91·3% respectively not losing a single day's work in the month. These figures are held to support "in a general way" the thesis that the application of a rigid and arbitrary retiring age is unjustifiable.

*R. J. Matthews*

# Industrial Medicine

1784. **An Epidemiological Study of Rheumatoid Arthritis Associated with Characteristic Chest X-ray Appearances in Coal-workers**

W. E. MIALL, A. CAPLAN, A. L. COCHRANE, G. S. KILPATRICK, and P. D. OLDHAM. *British Medical Journal* [*Brit. med. J.*] **2**, 1231–1236, Dec. 5, 1953. 5 figs., 22 refs.

In this epidemiological study, carried out by members of the Medical Research Council Pneumoconiosis Research Unit, of a syndrome recently described by Caplan (*Thorax*, 1953, **8**, 29) in which rheumatoid arthritis is associated with nodular fibrosis of the lung, chest radiographs of miners in the Rhondda Fach, South Wales, were re-examined. From among those showing massive fibrosis or tuberculosis, all films (20) which were thought also to show " rheumatoid "-type opacities were selected, 60 other films not showing these characteristics being used as controls. The 20 miners from whom the characteristic films were obtained were visited, questioned, and their joints examined if the history suggested arthritis; the criteria for the clinical diagnosis of arthritis are given. In addition, all men considered (in a previous survey) to have rheumatoid arthritis, as well as the 20 selected as having " rheumatoid " radiological appearances in the chest, were fully investigated.

It was found that the incidence of rheumatoid arthritis was higher (3%) among miners having massive fibrosis or tuberculosis than among the general population (0·42%), while its prevalence in the group showing " rheumatoid " opacities in the chest film was 55%. (No clinical evidence of rheumatoid arthritis was found in the whole series save in these two groups.)

The activity, severity, and duration of the arthritis were not correlated with the degree of typical " rheumatoid " radiological appearance. It was also noted that the rheumatoid lung lesions may either precede the onset of arthritis or develop subsequently. Total dust exposure may be a significant factor in determining the occurrence of rheumatoid arthritis, and it was noted that a high prevalence of arthritis occurred in men exposed to stone dust. Clinical examination of the group showed evidence of pulmonary tuberculosis in only one man.

One case in which the chest radiograph showed rheumatoid lesions came to necropsy during the investigation; the findings are detailed. The pulmonary lesions consisted of whorled, yellowish-white, collagenous fibrous tissue with central softening but no evidence of tuberculosis, and resembled those described by Gough under the name of " infective nodules ". Although the findings at this necropsy did not confirm the presence of tuberculous infection, 5 other necropsies of men with rheumatoid arthritis (in whom the *x*-ray appearances were less typical) have yielded evidence of it. Also, from 2 men with " rheumatoid " chest lesions and proved tuberculosis atypical bacilli were isolated which produced tuberculosis on injection into guinea-pigs. The condition may therefore be one in which the tubercle bacilli are modified.

In the discussion it is suggested that the hypotheses (*a*) that these appearances are coincidental and merely a manifestation of the rheumatoid syndrome, and (*b*) that the pathological changes play the part of a chronic septic focus, are equally unsatisfactory for reasons given. The authors conclude that there must be some other factor, and that the predisposition to form these lung lesions may be an expression of an unusual type of tissue reaction to dust and tuberculosis in miners who are predisposed to rheumatoid arthritis.

(The methods and criteria of examination and of evaluating observer-error are discussed in an appendix to the paper.) *L. W. Hale*

1785. **Cortisone in Pneumoconiosis with and without Reversible Bronchoconstriction**

M. C. S. KENNEDY. *Lancet* [*Lancet*] **1**, 77–79, Jan. 9, 1954. 17 refs.

At the Medical Research Council Silicosis Treatment Centre, Stoke-on-Trent, 12 patients with chronic lung disease, all but 2 of whom had radiological signs of pneumoconiosis, were observed before, during, and after treatment with 100 mg. of cortisone acetate daily by mouth for 14 days. Estimates of the maximum ventilatory capacity were made by measuring the expiration flow rate (E.F.R.); 7 patients whose E.F.R. increased by more than 10% after inhalation of 1:1000 adrenaline were considered to have " reversible bronchoconstriction ".

Although 8 of the 12 patients claimed subjective improvement of dyspnoea during and after cortisone therapy, the mean E.F.R. of the group both before and after adrenaline inhalation was unchanged. There was a slight but not significant fall in the mean erythrocyte sedimentation rate of the group at the end of the treatment. No radiological changes were seen and there was no evidence of activation of tuberculosis.

It is concluded that cortisone has no place in the treatment of bronchospasm in pneumoconiosis.

*C. M. Fletcher*

1786. **Histamine Content of the Blood in Silicosis and Pneumosclerosis of Chemotoxic Aetiology.** (Содержание гистамина в крови при силикозе и пневмосклерозах токсикохимической этиологии)

I. A. GEL'FON. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 75–76, Dec., 1953.

The author has determined the blood histamine level in 100 patients suffering from uncomplicated silicosis, silico-tuberculosis, and " pneumosclerosis of chemotoxic aetiology ", and in 23 control subjects without pulmonary disease. The normal blood histamine content ranges

from 0·02 to 0·08 μg. per ml. In the controls it was found to vary between 0·035 and 0·096 μg. per ml., in the cases of uncomplicated silicosis between 0·05 and 0·3 μg., in those with silico-tuberculosis between 0·04 and 0·346 μg., and in those with chemotoxic pneumosclerosis between 0·08 and 0·3 μg. per ml. The figures were higher in more advanced cases of pneumosclerosis.

Thus there is a marked increase in the histamine content of the blood in these diseases. This increase, in the author's view, is not specific for silicosis, but is a reflex response to an irritant. He also found that this change runs parallel with a rise in the albumin:globulin ratio in the blood which suggests that histamine exerts some influence on the permeability of the pulmonary capillaries. *L. Firman-Edwards*

1787. **Endogenous Haemosiderosis of the Lungs, a Disease Liable to be Confused Radiologically with Pneumoconiosis.** (L'emosiderosi polmonare endogena, una affezione radiologicamente confondibile con le pneumoconiosi)
E. C. VIGLIANI. *Medicina del lavoro* [*Med. d. Lavoro*] **45**, 1–11, Jan., 1954. 7 figs., 12 refs.

1788. **Perforation of the Nasal Septum Due to Soda Ash**
R. M. ARCHIBALD. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **11**, 31–37, Jan., 1954. 6 figs., 15 refs.

Soda ash (calcium carbonate or washing soda) is manufactured from coke, limestone, and brine, and the dried ash is mechanically packed into jute or paper bags. Dust is invariably produced at the packing points despite exhaust ventilation, and the soda ash causes rhinorrhoea and paroxysmal sneezing among the packers. Considerable dust is also raised in the cleaning and repairing of returned jute bags, of which many thousands may be handled in a day. Many of the workers are reluctant to wear protective masks.

In this study carried out at a large chemical works, two groups of workers, the ash-packers and the bag-plant workers, were compared with two control groups of workers, one consisting of patients who sought medical advice for any reason at the works surgery and the other of men who applied for employment at the works. Among 63 ash-packers, 5 cases of perforation of the nasal septum were found, and in 2 further cases thinning of the septum was so marked that perforation was obviously impending. The men with perforation were all aged between 40 and 49 and the period of exposure ranged from 15 months to 20 years. Among 156 workers in the bag-repairing shop there were 14 perforations of the septum and 5 impending perforations, 9 of these occurring in workers aged between 40 and 49, 6 in those between 30 and 39, and 3 in those between 50 and 59, the period of exposure here ranging from 5 to 19 years.

Among 200 employees attending the works surgery there were only 2 perforations and 11 cases in which atrophy of the nasal mucosa was demonstrated, while among 100 consecutive applicants for employment there were no cases of perforation. The incidence of perforation, therefore, in four groups of people with large, moderate, slight, and no exposure to soda-ash dust was respectively 11·1, 12·1, 1·0, and .0%. Soda ash may therefore be listed among the chemicals which give rise to perforation of the nasal septum, the most important of such substances being chrome and arsenical salts. Prevention of the disease would seem to rest with the engineer, who must find means to reduce the dust and, if possible, eliminate it. *K. M. A. Perry*

1789. **Pilot Trial of an Antihistaminic Drug in the Control of "Tetryl" Dermatitis**
W. A. BAIN and G. H. THOMSON. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **11**, 25–30, Jan., 1954. 9 refs.

The compound 2:4:6-trinitrophenylmethylnitramine (known commercially as "tetryl" and in the Services as C.E. (composition, exploding)) is an important intermediate detonating agent for high-explosive charges. Workers in ordnance factories manufacturing this substance, in addition to becoming yellow about the hands and face, are prone to develop dermatitis which is a cause of a large wastage of labour. The dermatitis usually develops 8 to 15 days after contact with the "tetryl". As the premonitory symptoms are usually either itching of the face and neck, progressing to erythema and urticaria, or rhinitis with respiratory discomfort suggestive of mild asthma, it seemed as if the onset of the condition was associated with the release of histamine, which might result either from a sensitization reaction or from "tetryl" acting as a simple histamine liberator.

In a study of the condition, carried out at the University of Leeds, the authors therefore decided to try the effect of antihistaminic drugs in some of the patients suffering from dermatitis. The preparation employed was chlorcyclizine hydrochloride ("histantin"), since it is not prone to produce sleepiness, which might be dangerous in a detonator shop; nevertheless, amphetamine was also given to control drowsiness during the first 2 days of the antihistaminic treatment. In all, 28 patients underwent this antihistaminic treatment, 16 other workers who received orthodox treatment with local applications acting as controls. Treatment was considered successful if the patients were able to continue work in heavy contact with tetryl. Among the 28 patients the antihistaminic treatment was successful in 26 and failed in 2, whereas among the 16 given the standard treatment there were 4 successes and 12 failures. In the standard-treatment group the average time required for signs and symptoms to clear was 16 days; in the chlorcyclizine-treated group, however, symptoms were cleared in an average of about 4 days and signs in about 6 days. The average dosage used in the treatment of the patients was 50 mg. of histantin twice a day.

This pilot trial was considered sufficiently successful to warrant an attempt at a more rigorous trial. This, however, had to come to an abrupt end, since the successful antihistaminic treatment led to a temporary solution of the labour problem among workers handling tetryl, and as no further people were entering this work, there were no further subjects with tetryl dermatitis in whom a

further trial could be conducted. The authors discuss some of the statistical and other defects unavoidable in the pilot experiment, but conclude nevertheless that the results give ample justification for a more rigorous and extended trial. *K. M. A. Perry*

1790. **An Experimental Study of the Objective and Subjective Aspects of Fatigue during Monotonous Work. I. Research on a Group of Students.** (Étude expérimentale des aspects objectifs et subjectifs de la fatigue pendant un travail monotone. I. Recherche effectuée sur un groupe d'étudiants)
C. GUGENHEIM. *Travail Humain* [*Travail hum.*] **16**, 219–240, July–Dec., 1953. 13 figs., 30 refs.

Tests were carried out on 14 female and 6 male students to determine the relation between subjective feelings of fatigue and objective criteria of performance of an unpaced, repetitive, aiming task (Lahy's punching-machine test). During the course of the test the subject indicated when he felt tired, and worked until he felt unable to continue because of fatigue or until he had completed 100 minutes' work. Counter records of speed and of accuracy were taken every minute.

Duration, speed, and accuracy of work all showed considerable individual differences. No correlations were made, but the subjects were classified into four groups each showing different tendencies. Group 1 showed great consistency both in speed and accuracy throughout the test and reported fatigue only during the last 20 minutes. The reported fatigue was not reflected in their counter scores. Group 2 were consistent in their output, but their accuracy scores showed marked and increasing scatter owing to a growing failure of muscular co-ordination. Group 3 were characterized by a gradual deterioration in consistency both as regards speed and accuracy. They reported subjective fatigue more frequently at the beginning of the test than at the end. Group 4 were highly irregular in speed and accuracy from the beginning, and soon gave up. The author concludes that the subjective and the objective manifestations of fatigue do not necessarily occur together. *R. Conrad*

1791. **Mental Health in Relation to the Labour Turnover of Unskilled Workers in a Large Industrial Establishment**
M. MARKOWE and L. E. D. BARBER. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] 7, 205–210, Oct., 1953. 9 refs.

An investigation was made by the Unit for Research in Occupational Adaptation of the Medical Research Council into stability of employment and its relation to mental health among 100 men aged 20 to 62 and 100 women aged 15 to 58 selected at random from those newly engaged for unskilled labour at two large Manchester factories. Each worker was interviewed, examined clinically, and given tests of intelligence (the dominoes test), ischaemic pain endurance, and exercise tolerance during the first week of employment.

The physical examination included measurement of height, weight, visual acuity, and haemoglobin level. The personality traits and mental health of each individual were assessed on 5-point scales, that for mental health ranging from Rating 1 (healthy, mature, vigorous, and well-integrated) to Rating 5 (definite disabling sickness needing treatment); Ratings 1, 2, and 3 covered the "normal" range, while persons with Ratings 4 and 5 were considered neurotic or psychologically handicapped. The ischaemic endurance test involved repeatedly clenching the fist after inflation of a sphygmomanometer cuff to a pressure of 250 mm. Hg.

The subsequent labour record was followed for 6 months, during which 21 of the men and 52 of the women left their employment. Significant correlations were found between leaving the job and neurotic mental-health rating, poor past employment record, emotional instability, and parental deprivation in the men, and between leaving and poor past employment record, poor pain endurance, and certain personality traits in the women. Extrovert women tended to leave, while conscientious and obsessional ones stayed. There also seemed to be some tendency for married men to be less, and married women to be more, disposed to leave. In the ischaemic test those women who left had a mean score of 146 seconds (standard deviation 4·79), while those who stayed had a mean score of 175 seconds (standard deviation 80·64). The high degree of variation in the latter was possibly due to the comparatively large number reaching the arbitrary maximum of 300 seconds. The ischaemic test showed no significant difference between those men who left and those who stayed.

Some psychological handicap (Ratings 4 and 5) was present in 43 of the men and 55 of the women, the majority being only mildly neurotic. The handicaps found among the men included anxiety states, depressive states, emotional instability, dullness, and feeblemindedness; among the women anxiety states, hypochondriasis, over-sensitive and suspicious traits, emotional instability, and inadequate personality. The intelligence scores of the men ranged from 5 to 35 points (maximum possible, 48), and of the women from 7 to 36, the mean values corresponding to I.Q. values of 91 for men and 89 for women. Among the men, 7 with normal ratings and 7 neurotics left in the first 10 weeks, and 7 more neurotics left between the 11th and 26th weeks; however, only 2 of the 9 with Rating 5 left. Among the women, 32 of the 52 who left and 23 of the 48 who stayed were neurotic; 14 of the 19 with Rating 5 left.

The authors comment on the striking fact that about half their population showed neurotic symptoms, and on the tendency of severely neurotic men to stay in their jobs and of severely neurotic women to leave. They also discuss the possible predictive value of the ischaemic pain endurance test in women and the difference between men and women in this respect. *J. F. Mackworth*

1792. **Use of Monocalcium Disodium Ethylene Diamine Tetra-acetate in Lead Poisoning**
H. L. HARDY, H. B. ELKINS, B. P. W. RUOTOLO, J. QUINBY, and W. H. BAKER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154**, 1171–1175, April 3, 1954. 2 figs., 11 refs.

# Anaesthetics

1793. **A Clinical Trial of Laudolissin as a Relaxant in 524 Cases**
J. W. DUNDEE, T. C. GRAY, and J. E. RIDING. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **26**, 13–21, Jan., 1954. 4 figs., 12 refs.

In this trial, reported from the Department of Anaesthesia, University of Liverpool, and carried out on 524 patients undergoing abdominal or thoracic operations, "laudolissin" (laudexium methylsulphate) was found to have many properties in common with D-tubocurarine, but differed from it in a few important respects. For example, relaxation adequate for tracheal intubation was not obtained for 3 minutes, but the total duration of action of the drug was appreciably longer than that of tubocurarine, thus making it valuable in cases where it is difficult to administer supplementary doses of relaxant during the operation. For closing the peritoneum at the end of long operations, when it is undesirable to give more of the relaxant, it was found that very small amounts of ether (just detectable by smell) appeared to have a truly synergistic effect and greatly enhanced the relaxing effect of laudolissin. Similarly, 10 to 20 mg. of gallamine triethiodide at this juncture was also unexpectedly effective.

Weight for weight, laudolissin appeared to be about half as potent as tubocurarine. Like that drug it was antagonized by neostigmine, but a warning is given that this antagonism is not complete; some 15% of the authors' patients required more than 5 mg. of neostigmine, and on 6 occasions the patient became "recurarized" after return to the ward. The conclusion is drawn that laudolissin is not a complete substitute for tubocurarine, but that it has a place in cases in which it is undesirable to give repeated injections of a relaxant during operation. *Donald V. Bateman*

1794. **The Effects of N-Allylnormorphine on Healthy Subjects Premedicated with Morphine**
J. P. PAYNE. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **26**, 22–25, Jan., 1954. 1 fig., 9 refs.

The advantages of a specific antidote to morphine are self-evident. At Manchester Royal Infirmary the author therefore investigated the value of N-allylnormorphine in antagonizing the effect of morphine given to 4 outpatients preparatory to cystoscopy. Because of the untoward effects on these patients, the investigation was continued on 7 healthy volunteer male subjects. The initial dose of morphine was ¼ grain (16 mg.) in all cases, and N-allylnormorphine was given intravenously in doses of 10 mg.

It was found to stimulate respiration, as measured by a spirometer, for 3 or 4 minutes, but thereafter the effect rapidly disappeared and the minute volume fell to below the control level. In addition, there were unpleasant side-effects. Extreme drowsiness was constant in all the subjects, lasting for several hours and being accompanied in most instances by pallor, sweating, nausea, and even vomiting. The two series studied were admittedly small, but the effects were quite unmistakable and the author concludes that the hypnotic and emetic effects of the drug will prevent its use as an antagonist to morphine, certainly in out-patients. *Donald V. Bateman*

1795. **Neurological Complications following the Use of Efocaine**
W. K. NOWILL, H. HALL, and C. R. STEPHEN. *Archives of Surgery* [*Arch. Surg. (Chicago)*] **67**, 738–740, Nov., 1953. 10 refs.

Three cases have been presented in which spinal cord complications followed the use of "efocaine". These complications consisted of transverse myelitis in 2 cases, and Brown–Séquard syndrome in one case, and followed intercostal nerve block in one, and sympathetic nerve block in 2 cases.

Since these complications are of such serious nature, the use of efocaine should probably be limited to those areas where possible tissue damage is unimportant.—[Authors' summary.]

1796. **Vascular Dynamics in Controlled Hypotension: a Study of Cerebral and Renal Hemodynamics and Blood Changes**
G. C. MORRIS, J. H. MOYER, H. B. SNYDER, and B. W. HAYNES. *Annals of Surgery* [*Ann. Surg.*] **138**, 706–711, Nov., 1953. 2 figs., 15 refs.

Although controlled hypotension in surgery, and particularly in neurosurgery, is now widely used, little work has been done in investigating the changes in vascular dynamics which occur, for example, in such important organs as the brain and kidney as a result of this procedure. The authors, working at Baylor University College of Medicine, Houston, Texas, have sought therefore to determine the lowest blood pressure level which may be safely induced in controlled hypotension. To this end they measured the cerebral blood flow and cerebral oxygen consumption, the differential renal function, and blood volume in a group of surgical patients in whom marked hypotension had been induced by administration of hexamethonium. The patients lay horizontally supine and were given a continuous intravenous infusion of 500 mg. of hexamethonium chloride in one litre of a 5% solution of glucose in water. They were not anaesthetized, so that any untoward effects of hypotension could be more readily detected. The blood pressure was continuously recorded from a needle in the femoral artery.

Cerebral blood flow was determined by the nitrous oxide method on 5 normotensive and 3 mildly hyper-

tensive subjects. When the mean blood pressure of the group was 61% of the control level after one hour's infusion, the mean cerebral blood flow in ml. per 100 g. of brain tissue per minute was 70% of the control value, while cerebral oxygen consumption was 88% of the pre-test value and cerebral vascular resistance was 89% of the control. Arterial blood *p*H was not changed significantly and changes in arterial carbon dioxide partial pressure were inconstant and erratic.

Renal function studies were carried out on 12 subjects, inulin clearance being used to measure glomerular filtration rate (G.F.R.), and 2 to 4% PAH to measure renal plasma flow (R.P.F.). Control determinations were expressed as averages of three 10-minute periods. Observations were taken after ½, 1, 2, and 3 hours, the results being expressed as averages of 2, 3, or 4 10-minute periods. The mean blood pressure fell to about 67% of the control level. For the four periods of observation the G.F.R. values were 74%, 76%, 83%, and 78% respectively of the control value. R.P.F. values, however, after an initial fall, rose steadily and were 74%, 89%, 105%, and 124% respectively of the control value. Thus filtration fraction values decreased progressively, being 121%, 90%, 82%, and 67% respectively. Urinary volumes were markedly reduced during the entire period, the figures for the four test periods being 20%, 21%, 16%, and 15% of the control volume.

The blood volume was measured in 16 patients before the induction of hypotension, and one hour after in 11 of them and 2 to 4 hours after in 5, by the intravenous injection of 5 ml. of radioactive iodinated human serum albumin (10 $\mu$c. of $^{131}$I per ml.), 10 ml. of arterial blood being collected 15 to 20 minutes later and radioactivity observed in a Texas well counting chamber. The mean plasma volume was found to be increased by 17%, the total blood volume by 12%, and the erythrocyte mass by 5%. The authors suggest that the blood volume increases because of the lowered capillary hydrostatic pressure and also through utilization of the plasma envelope surrounding the axial stream of corpuscles. In the 16 patients studied, gradual losses of blood during operation up to 600 ml. were well tolerated. The authors conclude that there is little danger of cerebral or renal anoxia in a supine patient under controlled hypotension induced by hexamethonium, as long as the blood pressure is not allowed to fall below 55 mm. Hg.

*B. L. Finer*

1797. **A Technique for the Production of Hypothermia. Preliminary Report**

C. B. Ripstein, C. E. Friedgood, and N. Solomon. *Surgery* [*Surgery*] **35**, 98–103, Jan., 1954. 6 figs., 7 refs.

By the use of hypothermia the heart can be excluded from the circulation long enough for an intracardiac operation to be performed without causing irreversible damage to the brain, since in hypothermia the metabolic needs of the tissues are greatly decreased. The production of hypothermia by the application of cold alone needs much time and deep anaesthesia, is exhausting to the patient, and moreover may lead to difficulty in re-warming. It has been shown, however, that the anti-histaminic, chlorpromazine, inhibits the thermoregulatory centre in warm-blooded animals. In this paper from New York University School of Medicine the authors describe their method. The subject is anaesthetized with thiopentone and curare and intubated, and is then placed in refrigeration blankets through which alcohol solution at 30° F. (−1° C. is circulated. Chlorpromazine is given in doses of 50 mg. intravenously and 100 mg. intramuscularly, followed by a further dose of 50 mg. intramuscularly every 1 or 2 hours. Light anaesthesia is continued with thiopentone, and the rectal temperature is continuously recorded.

When body temperature reaches 80° F. (26° C.) the refrigerant fluid is warmed to 70° F. (21° C.) Most complications reported so far have occurred below 80° F., and this is therefore taken to be the limit of safety. Rewarming can be carried out at any time by injecting 50 mg. of chlorpromazine intramuscularly and raising the temperature of the fluid to 110° F. (43·5° C.).

In the dog and in man the temperature begins to fall immediately, and drops in a smooth curve to 80° F. in 15 to 45 minutes without causing shivering. If the drug is used without the refrigeration blanket the temperature falls only to 92 to 94° F. (33·5 to 34·5° C.) and stays there.

In dogs the heart has been excluded from the circulation for periods up to 15 minutes with no evidence of cerebral damage on recovery. The right atrium has been opened and interatrial septal defects created and repaired. Direct suture has been used for small defects and a pedicle flap of the auricular appendage for large openings. This procedure has carried a 25% mortality, death being due to irreversible ventricular fibrillation.

In the authors' opinion cardiac surgery under hypothermia should be attempted only in desperate cases in which there is little chance of survival otherwise. Three of their patients undergoing exploratory cardiotomy died. Of 17 other patients treated by artificial hibernation for the control of hyperpyrexia or to relieve intractable pain, all recovered. Cardiac irregularities developed in 2 cases, but these were reversed on re-warming. The authors conclude that hypothermia is of limited application at the present time, and that further experimental work is necessary to make this a reasonably safe procedure.

*W. Stanley Sykes*

1798. **A Convenient Apparatus for Providing Controlled Hypothermia**

J. M. Inglis, W. H. Biffen, and A. L. d'Abreu. *Lancet* [*Lancet*] **1**, 549–550, March 13, 1954. 2 figs., 6 refs.

1799. **The Evaluation of Pentylenetetrazol as a Barbiturate Antagonist**

J. F. Fazekas and T. Koppanyi. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **33**, 58–63, Jan.–Feb., 1954. 13 refs.

1800. **Concentrations of Diethyl Ether in the Blood of Intubated and Non-intubated Patients**

A. Mackenzie, E. A. Pask, and J. G. Robson. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **26**, 111–117, March, 1954. 6 figs., 4 refs.

# Radiology

## RADIOTHERAPY

1801. **The Choice of Treatment for Sarcoma of the Tonsil.** (Hinweise zur Behandlung des Tonsillen-Sarkoms)
H. TRÜBESTEIN. *Strahlentherapie* [*Strahlentherapie*] **92**, 281–296, 1953. 20 refs.

Details are given of 52 cases of sarcoma of the tonsil treated in the past 23 years at the University Röntgen Institute, Frankfurt-am-Main. Histological confirmation was obtained in 39 cases, 17 of which were round-cell sarcomata, 15 lymphosarcomata, 5 reticulosarcomata, 1 spindle-cell carcinoma, and 1 myxosarcoma. There was involvement of the regional lymph nodes at the start in 59%. The tumour is usually ulcerated and may be confused with Vincent's angina; lymphosarcoma, however, is usually not ulcerated and the appearance may resemble that of a peritonsillar abscess.

The technique of irradiation is described. Various methods of fractionation were used, with 5 fields—one tonsillar and one submental on each side, and one on the cheek of the affected side. If there were no involved nodes at the angle of the jaw the field size was $6 \times 8$ cm. and if such nodes were present, $8 \times 10$ cm. or, rarely, $15 \times 10$ cm. The importance of adequate dosage is stressed—a total surface dose of at least 6,000 r in 20 days (or its biological equivalent for other periods) is necessary. Long survival was achieved only in cases without metastases or with unilateral metastases. Bilateral lymph-node metastases almost invariably indicate generalization, and no such patient in this series survived 6 months, even with high dosage. However, even with widespread disease the condition can be improved by adequate local dosage to the regions involved. Operation can be dispensed with, as it adds nothing to the long-term results, but if it is performed, then post-operative radiation should be given in the same dosage. Neither surgery nor adequate irradiation appears to encourage metastasis, but low dosage allows secondary growth to appear in as little as 2 months, compared with at least a year after high dosage. *J. Walter*

1802. **Cathode Ray Treatment for Lymphomas Involving the Skin**
H. F. HARE, J. L. FROMER, J. G. TRUMP, K. A. WRIGHT, and J. H. ANSON. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **68**, 635–642, Dec., 1953. 5 figs., 5 refs.

The authors describe exploratory attempts made at the Massachusetts Institute of Technology and Lahey Clinic, Boston, to use a high-energy cathode-ray (electron) beam in the treatment of extensive malignant disease of the skin. The rays were produced by a Van de Graaff type of generator at 2·5 megavolts, but it is pointed out that the penetration of the rays can be altered at will by varying the voltage. The rays, discharged into the air, are made to pass through an elongated slit in an aluminium cone from which they emerge in a narrow, slit-like beam which covers a field 5 mm.$\times$45 cm. This beam, its long axis transverse to the body of the patient, remains stationary while the patient is passed beneath it on an electrically-driven couch, first supine, then prone, then successively on right and left sides. In this way the whole skin area can be irradiated, only the eyes being protected by suitable goggles. The important characteristic of this electron radiation is that its maximum intensity is reached some 4 mm. below the skin surface, yet none of the rays penetrate farther than about 12 mm. In this way not only are the deeper tissues completely spared, but most of the sweat glands escape also.

Five patients suffering from reticuloses affecting the skin were selected for treatment. They were given a daily dose at first equivalent to about 140 r to the whole body surface. After a fortnight, treatment was continued at weekly intervals until most patients had received a total dose of 2,000 r.e.p. in about 10 weeks. There was complete disappearance of extensive lesions of mycosis fungoides, and the patients remained well between 6 and 18 months after treatment. Two patients developed blood changes of a " pantocytopenic " type which, however, responded satisfactorily to treatment. The cause of these changes, which were unexpected in view of the non-penetrating character of the radiation, is still under study. *E. Stanley Lee*

1803. **Radiotherapy of Epibulbar Malignant Melanomata**
M. LEDERMAN. *Transactions of the Ophthalmological Society of the United Kingdom* [*Trans. ophthal. Soc. U.K.*] **73**, 399–413, 1953. 5 figs., 4 refs.

The results of a series of 21 cases of epibulbar malignant melanoma treated by radiotherapy at the Royal Cancer Hospital, London, are discussed, the methods employed are described and, although it is emphasized that the series is a small one, the following conclusions are drawn.

The general view that all malignant melanomata are radioresistant is open to question, at least as regards the epibulbar variety. Of the three types of the latter, limbal tumours are comparatively radiosensitive and can be satisfactorily treated with $\beta$ radiation, if necessary without preliminary surgical removal. Tumours of the bulbar conjunctiva are less sensitive and their treatment should be preceded by surgical removal. Treatment with $\beta$ radiation is adequate in the case of small tumours, but for large ones $\gamma$ irradiation of the whole conjunctival sac is necessary; melanomata of the cutaneous and mucous surfaces of the lids are radioresistant. *A. Lister*

See also Haematology, Abstract 1660.

## RADIODIAGNOSIS

1804. **The Technique of Cinedensigraphy.** (Technique de la ciné-densigraphie)
M. MARCHAL. *Presse médicale* [*Presse méd.*] **61**, 1734–1736, Dec. 25, 1953. 4 figs., 30 refs.

An account is given of the technique of "cinedensigraphy", which is a modification of electrokymography applied to the lung fields whereby the vascular pulsation of any part of the lung may be recorded in the form of a graph. It is claimed that the instrument is more sensitive than the unaided eye at fluoroscopy and that it records not only pulsation of the larger blood vessels, but also the rhythmic change of density of the peripheral lung fields. It is used in conjunction with an electrocardiograph, and a second photo-electric cell is used to obtain a simultaneous electrokymographic record of the ventricular or main arterial excursions.

A very brief outline is given of the method of interpretation of the graph obtained, and the means whereby transmitted pulsation from the heart and main vessels, which is superimposed upon the change of density of the lung, may be recognized and subtracted from the graphic curve are outlined. The extra wave produced by ventricular pulsation is easily recognizable, but the process of making allowance for the effect of the larger vessels near the lung hilum is rather more complicated.

The examination is not exhausting to the patient, and does not involve giving a large dosage of *x* rays.

*G. H. Du Boulay*

1805. **The Application of Cinedensigraphy to the Investigation of Tumours of the Lung.** (Application de la cinédensigraphie à l'exploration des tumeurs du poumon)
A. RAVINA, M. MARCHAL, and M. PESTEL. *Presse médicale* [*Presse méd.*] **61**, 1736–1737, Dec. 25, 1953. 4 figs.

A report is presented of 5 cases examined by the electrokymographic technique described by one of the authors as "cinedensigraphy" [see Abstract 1804]; a sixth case is also cited in order to show the sensitivity of the method in detecting the vascular pulsation of the lungs. In all the first 5 cases a pulmonary, paramediastinal mass was observed on the radiograph and bronchoscopy failed to provide a definite diagnosis. In 3 cases the mass was subsequently diagnosed as bronchial carcinoma (in 2 at necropsy and in one from the development of the disease). The other 2 patients do not appear to have had bronchial carcinoma, although thoracotomy was not performed; in one of them the mass persisted unchanged for several years, and in the second the mass subsequently disappeared completely.

In the 3 cases of bronchial carcinoma vascular pulsation in the lung on the affected side was much less marked than on the unaffected side, this loss of vascular pulsation extending far beyond the limits of the radiographic shadow and involving the greater part, or the whole, of the lung field. In the 2 cases without bronchial carcinoma, on the other hand, the vascular pulsation in the whole of the lung on the affected side beyond the immediate limits of the mass was normal and of a degree comparable with that seen in the healthy lung. The case illustrating the sensitivity of the apparatus was that of a patient with a large congenital cyst of the lung in which no vascular markings could be detected on a plain radiograph and no opacification seen on angiopneumography. Nevertheless, cinedensigraphy disclosed vascular pulsation in the translucent area.

The authors conclude that the method is of great value in distinguishing between malignant tumours (in which the loss of vascular pulsation is widespread on the side of the lesion), and benign tumours (in which there is little change in the vascular pulsation in the peripheral lung fields).

[It is probable that in Great Britain some at least of these patients would have come to thoracotomy and it would not have been of quite such vital importance from the prognostic point of view to make a radiological diagnosis.] *G. H. Du Boulay*

1806. **The Radiological Diagnosis of Erosive Gastritis.** (Die Röntgendiagnose der Gastritis erosiva)
W. ABEL. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **80**, 39–50, Jan., 1954. 12 figs., 24 refs.

A long introductory discussion of erosive gastritis and its *x*-ray diagnosis [based largely on the pre-1939 German literature] is followed by brief notes on 7 patients, whose ages ranged from 16 to 43, examined at the Evangelical Hospital, Oldenburg. Gastrectomy was performed on 5, presumably on account of the associated chronic ulcer, and photographs of the specimens are presented side by side with the [beautifully reproduced] radiographs. The rounded filling defects in the films are thereby shown to correspond with wart-like protuberances of the mucosa, and the minute central fleck of barium to an erosion on the summit. The histology is described in each case [but it is not always easy to follow the description and no photomicrographs are reproduced]. In some cases the protuberances are said to be mainly the result of oedema and inflammation around the erosions; in others they are described as islets of chronically inflamed mucosa. Polymorphonuclear leucocytes are stated to have been numerous in the inflamed areas and there were also lymphocytes and plasma cells. The symptoms were those of partial pyloric blockage, with colicky pain and marked acid regurgitation. Hypochlorhydria was usual even in the presence of an associated duodenal ulcer. Epigastric tenderness was often marked.

[No dates are given in the histories and there is no hint as to how often the author sees such cases. In Great Britain they are uncommon and the abstracter has been unable to find a radiological colleague who can produce films which are comparable to those reproduced. This may, however, be due in part to differences of technique.]

The author states that for the demonstration of erosive gastritis it is essential to have a freely flowing, aqueous suspension of colloidal barium sulphate without added colloid, the exposure must be less than 0·05 second, and the films must be taken at once without undue compression or massage of the stomach.

*Denys Jennings*

# History of Medicine

1807. **Charles Turner Thackrah in the Agitation for Factory Reform**

G. ROSEN. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 285–287, Oct., 1953. 1 fig., 12 refs.

Charles Turner Thackrah, born in Leeds on May 22, 1795, was destined for the Church but decided to study medicine, and in 1811 he began a three-year apprenticeship to a Leeds surgeon. In 1814 he became a student at Leeds Infirmary, and in the winter of 1815–16 attended Guy's Hospital, where he was a member of the Physical Society and attracted the notice of Sir Astley Cooper. He devoted extremely long hours to study, and early began to keep a systematic record of cases; but he also found time to read widely, chiefly in medicine and history. In 1816 he qualified at the Apothecaries' Hall and at the Royal College of Surgeons, and in the following year set up in practice in Leeds.

In 1819 he published *An Inquiry into the Nature and Properties of the Blood, in Health and Disease*, which won a prize given by Sir Astley Cooper. He also took an interest in medical education, and in 1820 joined other young physicians in arranging lectures for pupils. In 1827 he completed the first lecture course on anatomy to be given in Leeds; these lectures were continued in 1828 but the College of Surgeons and the Apothecaries' Hall refused to recognize his certificates. In 1831 he co-operated in the establishment of the Leeds Medical School and he lectured there on anatomy, physiology, pathology, and surgery until 1833.

Thackrah was early brought into contact with problems of social medicine when he was elected town surgeon of Leeds and when he undertook to report to the managing committee of the Leeds workhouse on lodging-houses for the poor. He had begun to study the influence of manufacturing processes on the worker's health in 1824, when the movement leading to the Reform Act of 1832 was at its height and when industrial workers were beginning to demand improvement in factory conditions and restriction of child labour. In 1831 he published his pioneer work, *The Effects of Arts, Trades, and Professions, and of Civic States and Habits of Living, on Health and Longevity*. This work was favourably received and went into a second edition in 1832; it was quoted by Richard Oastler, whom Thackrah knew and supported, in his campaign for a ten-hour working day, and by Michael Sadler, who introduced the Ten Hours Bill into Parliament in 1831. Thackrah supported this Bill at a public meeting in Leeds, speaking with eloquence of his child patients. During the cholera epidemic of 1831–2 he visited Newcastle and Gateshead and published a pamphlet on the results of his investigations. In 1833 his health, always poor, deteriorated and he died on May 23 of that year.

Thackrah stands out among his contemporaries for his recognition of the social responsibility of the physician and his contribution, based on wide research, to the study of occupational health in Great Britain. In 1897 John Simon wrote of him: "One very important new line of thought in Preventive Medicine was opened for England in 1831 by Mr. C. Turner Thackrah. . . . By his eminently trustworthy book he . . . made it a matter of common knowledge, and of State responsibility, that, with certain of our chief industries, special influences, often of an evidently removable kind, are apt to be associated, which, if permitted to remain, give painful disease and premature disablement or death to the employed persons".

*W. J. Bishop*

1808. **The Complementary Careers of Michael Servetus: Theologian and Physician**

C. D. O'MALLEY. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **8**, 378–389, Oct., 1953.

The dual nature of Michael Servetus is revealed by the fact that he was condemned and burnt to death at Geneva in 1553 for theological views expressed in his book, *Christianismi restitutio*, a work which also contained the first printed description of the pulmonary circulation.

Servetus was born in Spain about 1511. His advanced theological views and medical knowledge were derived from a literal study of the Bible and the purified Greek text of Galen. He studied theology at Toulouse and received his early medical education at Lyons, where he was the friend of the physician, Symphorien Champier. He appears to have worked as a corrector to a publishing house in Lyons, and it seems likely that he read several of the works of Galen during this time. Between 1534 and 1539 he displayed his versatility in Paris, where he studied mathematics, medicine, and astrology, and his published works included an edition of Ptolemy's *Geography*, a medico-theological *Apologia* against the Tübingen physician, Leonard Fuchs, and his longest strictly medical book, *On Syrups*. It is suggested that this last work, with its description of the blood as the vehicle of bodily nourishment, possibly contains "the germ of the idea of the circulation".

Servetus left Paris in 1539, and thereafter practised medicine in Charlieu, Lyons, and Vienne, but his interest in theology reasserted itself. After a violent controversy with Calvin, he published his views in the secretly printed *Christianismi restitutio*. In his description of the pulmonary circulation, Servetus remained a Galenist, only shifting emphasis when he declared that the blood passed from the right to the left ventricle by way of the lungs, though a little might still pass through the septum of the heart. It is suggested that his motive in opposing the Galenical tradition was theological, since he believed that the divine spirit was infused into the blood in the lungs and was carried thence throughout the body.

*F. M. Sutherland*

1809. **New Light on Lady Mary Wortley Montagu's Contribution to Inoculation**
R. HALSBAND. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **8**, 390–405, Oct., 1953.

The part played by Lady Mary Wortley Montagu as a pioneer advocate of smallpox inoculation (or variolation) is examined in detail. Her interest in smallpox prevention was probably engendered by a disfiguring attack of the disease in 1715 at the beginning of her career at the court of George I. She accompanied her husband when he went to Turkey as ambassador in 1716, and was very impressed with the success of the local practice of " ingrafting " smallpox. A description of this practice had already been sent to the Royal Society in London by two physicians resident in Turkey, Emanuel Timoni in 1713 and Jacob Pylarini in 1715. In 1718, the Montagu's 4-year-old son was inoculated successfully by Charles Maitland, the surgeon who accompanied them to Constantinople.

In 1721, after their return to England, a severe smallpox epidemic broke out, and interest in inoculation was aroused when it was performed successfully on Lady Mary's daughter and on the two daughters of the Princess of Wales. There was considerable controversy over the practice, however, because of a number of failures and the opposition of certain sections of the clergy and the medical profession. To counter this opposition, Lady Mary, under the pseudonym " Turkey Merchant ", wrote an essay which was published in a London newspaper, *The Flying-Post: or, Post-Master*, in September, 1722. The editor toned down the force of her argument considerably before publication, and Lady Mary's original draft, as recovered from her family papers, is reproduced in the present article for the first time.

Opposition to smallpox inoculation continued, but died away in face of the widespread success of the practice, which became commonly accepted in Britain and abroad during the 18th century. *F. M. Sutherland*

1810. **Charles de Lorme, Physician to the Baths of Bourbon-l'Archambault (1584–1678).** (Charles de Lorme, médecin des bains de Bourbon-l'Archambault (1584–1678))
P. PIZON. *Presse médicale* [*Presse méd.*] **61**, 1786–1788, Dec. 25, 1953. 4 figs.

The dominant characteristic of Charles de Lorme that emerges from this biographical sketch is a flamboyant self-confidence which is typical of the French scene in the age of Henry of Navarre and Richelieu; his claim to medical fame rests on his share in the development of hydropathy and, in particular, of the spa at Bourbon-l'Archambault, near the now more famous town of Vichy.

Born in 1584, the son of Jean de Lorme, physician to Henry IV and Louis XIII, he received his medical education at Montpellier, where he graduated in 1607. His only published work consists of his collected theses, issued under the title of *Lauriers de l'orme* in 1608. He practised in Paris, with intervals for service with the army before La Rochelle and for diplomatic missions in Italy. His exaggerated styles of dress and speech and his brusque and violent treatment of patients and fellow-doctors made him a prominent figure in medical and court circles. In 1633 he was appointed to administer the spa at Bourbon-l'Archambault. The baths already existed and he proceeded to develop the buildings and facilities. Success was assured by a large number of aristocratic patrons, whose visits de Lorme was quick to publicize. His heated advocacy of the Bourbon waters, however, not unnaturally irritated influential sections of the medical profession. Details of his private life are given which well illustrate the kind of man he was; for example, a graphic picture is painted of his morbid fear of draughts in later years and the fantastic precautions he took to combat them.

After he died, on June 24, 1678, the buildings and equipment of the spa at Bourbon-l'Archambault remained substantially unaltered until the 19th century.
*F. M. Sutherland*

1811. **Mr. Johns Hopkins and Dr. Macaulay's " Medical Improvement "**
J. C. FRENCH. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **27**, 562–566, Nov.–Dec., 1953.

1812. **James Lind: Laudatory Address**
S. DUDLEY. *Proceedings of the Nutrition Society* [*Proc. Nutr. Soc.*] **12**, 202–209, 1953. 6 refs.

James Lind, Physician to the Fleet in the latter half of the eighteenth century, was a pioneer and an original investigator in three important fields, scurvy, hygiene, and tropical medicine. On each of these subjects he wrote a book which has become a classic. By banishing scurvy and typhus from the Royal Navy Lind was credited with having doubled its fighting force, and " it is therefore no idle fancy to assert that Lind as much as Nelson broke the power of Napoleon ". Probably the first deliberate, properly controlled, clinical therapeutic trial on record was Lind's experiment in which he demonstrated that patients given lemon juice were cured of scurvy, whereas the controls were not.

His powers of accurate observation led him more than any other pre-Mansonian physician to associate tropical fevers with stinging insects, and in his book on tropical medicine he recommends the choice of high, dry ground as the site for a dwelling place, with the clearance of scrub and efficient drainage. Similarly, he associated typhus fever—with scurvy the scourge of seamen—with vermin in the infested clothes of the press-gang's victims, and the delousing instructions which he drew up were not improved upon until the advent of DDT.

Lind was the first hygienist to note the relative freedom of ships from tropical diseases, and he therefore pleaded for the routine use of vessels moored off the coast as " health resorts ", a proposal which has never recommended itself to the naval authorities but has been repeatedly shown to be sound in practice when circumstances have forced its adoption.

In his book on tropical medicine he pointed out that the ignorance of commanders-in-chief concerning the maintenance of the health of their troops might cause the loss of thousands of lives, and " the history of the

fighting services proves over and over again Lind's inference, that the executive commanders must be health experts ". *Ruth Hodgkinson*

1813. **Early Investigations of Scurvy and the Anti-scorbutic Vitamin**

H. CHICK. *Proceedings of the Nutrition Society* [*Proc. Nutr. Soc.*] **12**, 210–219, 1953. 42 refs.

Scurvy was possibly known in the Hippocratic period and certainly at the time of the Crusades. In medieval England a large part of the population probably suffered from mild scurvy in late winter and spring, and through the ages it was a common and dreadful menace to all seafarers. Throughout its history there was a wealth of evidence that the disease was caused by lack of fresh fruit and vegetables, but even Lind's famous exposition of the subject was misunderstood and rejected by many, so that new theories of its cause and cure continued to be suggested by other authorities right up to the twentieth century. If Lind recognized the cause of scurvy and suggested the correct means of its prevention and cure, credit for the successful practical application of these measures goes to Captain Cook who, on his second voyage to the South Pole, 1772–5, obtained a supply of fresh fruit and vegetables whenever he touched land and was well-stocked with celery, scurvy grass, and *Sauerkraut*. Cook received the Copley medal of the Royal Society, not for his navigational discoveries, but for his success in maintaining so long a voyage without a death from scurvy among his crew. He himself regarded this as the greater feat.

But despite this and other demonstrations, and although Lind devoted his energies to securing a regular issue of lemon juice in the Royal Navy, it was not until 1795 [a year after his death] that success was achieved. The result was that by the beginning of the nineteenth century scurvy had virtually vanished from the Navy. Unfortunately, many mistakes were made subsequently, the most notable perhaps being the substitution of limes for lemons in many cases, with tragic consequences since the former fruit is not an effective antiscorbutic.

The first experimental investigations of scurvy were made early in this century by Holst and his colleagues on guinea-pigs, the presence of an antiscorbutic principle in green food being confirmed and many of its properties being defined. During the first world war the Lister Institute in London undertook a study of the disease at the instance of the military authorities with the prime aim of obtaining quantitative information about the distribution of the antiscorbutic vitamin among different vegetables and fruits and of discovering some potent and stable source suitable for transport. These trials confirmed the work of Holst and Frölich, revealed that raw cabbage was the equal of fresh lemon juice, and showed that dried herbs and vegetables were useless for the prevention of human scurvy, as was lime juice.

One type of scurvy, the infantile, may be considered a disease of modern times, since it was unknown until artificial feeding became a common practice at the end of the nineteenth century. Outbreaks also occurred in times of war when infants had to be fed on cereal gruels or when scanty milk supplies had to be heated to prevent souring. Now that it is a recognized rule that an extra source of ascorbic acid, such as orange juice, is indispensable for artificially fed babies, scurvy of this last type no longer exists today in Western countries.

*Ruth Hodgkinson*

1814. **Achievements of Chinese Medicine in the Ch'in (221–207 B.C.) and Han (206 B.C.–219 A.D.) Dynasties**

LEE T'AO. *Chinese Medical Journal* [*Chin. med. J.*] **71**, 380–396, Sept.–Oct., 1953. 4 figs., bibliography.

The Ch'in and Han dynasties were periods of great expansion in Chinese history, and this expansion was especially apparent in the field of medicine. The author of this paper, writing from Peking Medical College, describes in considerable detail some of the notable advances in the medical art. After describing the social background of the period, he gives an account of the advances achieved in diagnosis. Cholera, rheumatism, and smallpox were clearly defined at this time, as well as malaria and typhoid. Details of epidemics from the *Handbook of Remedies* are recorded, and among other diseases there described are trigeminal neuralgia, diabetes, cerebral haemorrhage, carbuncle, leprosy, cancer, and tetanus. Polycoria, glaucoma, and blepharitis are also mentioned and some account of the *Book of Rites* and the *Shuo Yuan* is given.

The diagnostic methods, as seen from descriptions in the *Su Wen*, are discussed at length and considerable space is given to Chang Chung-Ching's important *Treatise on Fevers*. The spread of the Chinese theory of the pulse to the Japanese, Arabs, and Hindus is noted. A section on formularies records the use of rhubarb, aconite, almond, gourd, ginger, cinnamon, mercury, and sulphur. In a discussion of the work of outstanding physicians, the names of Ch'unyu Yi, Chang Chung-Ching, Hua Tuo, Wu P'u, and Li Tang-Chih appear. A useful review of the medical works of the period makes reference to the lost *Huang Ti Nei Ching*, the *Wai Ching*, *Pai Shih Nei Ching*, *P'ang P'ien*, including extracts from the *Han Annals*. Finally, the status of doctors and the social conditions of practice in this remote period are described in this excellent article. A useful if somewhat limited bibliography is given.

*Calvin P. B. Wells*

1815. **The First Cylinder of Gas**

M. H. A. DAVISON. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **26**, 40–41, Jan., 1954. 1 fig., 1 ref.

1816. **The Mill Reek and the Devonshire Colic**

A. MEIKLEJOHN. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **11**, 40–44, Jan., 1954. 9 refs.

1817. **A History of Infant Feeding**

J. W. BURGESS. *University of Michigan Medical Bulletin* [*Univ. Mich. med. Bull.*] **19**, 324–333, Dec., 1953. 2 figs., 5 refs.

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